VOLUME 17 NUMBER 5

ARCHIVES
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MAY 1928

PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN STREET, CHICAGO, ILLINOIS. ANNUAL SUBSCRIPTION, $5.00

Entered as Second-Class Matter, October 30, 1917, at the Postoffice at Chicago, Illinois, Under Act of Congress of March 3, 1879. Accepted for mailing at special rate of postage provided for in Paragraph (Sec. 412, Act of October 3, 1917, authorized [illegible]

Archives of Dermatology and Syphilology

VOLUME 17 MAY, 1928 NUMBER 5

INDUSTRIAL DERMATOSES

GENERAL CONSIDERATIONS *

HARRY R. FOERSTER, M.D.

MILWAUKEE

Early in the sixteenth century, Paracelsus and Agricola recorded scabby and impetiginous skin disorders and ulcerations in those engaged in metal work and in salt mining. Since that day, the scope of occupational skin diseases has steadily increased, and they are encountered in practically every field of industry. It is pertinent, therefore, to study these diseases as a group, a dignity to which their importance entitles them, and to consider some of the problems presented by this subject to the dermatologist.

The first real contribution to occupational dermatoses was made in the year 1700 by Ramazzini, referred to as the father of industrial hygiene.[1] He described with considerable accuracy the dermatoses of washerwomen, bakers, farmers and of a host of other artisans. It is interesting to note that more than 200 years after bakers' dermatitis was first described by him, its exact etiology is still in dispute. R. P. White [2] recently expressed the opinion that it is an incident rather than a consequence of the trade; DeJong [3] thought it may be due to an idiosyncrasy to salt; Tankard [4] attributed it to potassium persulphate, a "flour improver," and others believe that sugar, tartrates and miscellaneous baking ingredients are etiologic factors. Mummery [5] considered "bakers' itch" a definite dermatitis peculiar to the baking and confectionery industry, and has isolated a yeastlike organism and has produced the disease in himself by inoculation. About 1924, the secretary of the Bakers' and Confectioners' Union of England reported a twenty-fold increase in bakers' eczema within a few years. This statement was

* Read at the Fiftieth Annual Meeting of the American Dermatological Association, Baltimore, May 12-14, 1927.

1. Ullmann, Oppenheim and Rille: Die Schaedigungen der Haut durch Beruf und gewerbliche Arbeit, Leipzig and Hamburg, Leopold Voss, 1915, vol. 1, pp. 1, 16 and 38; 1922, vol. 1, p. 296; 1925, vol. 2, pp. 1 and 51.

2. White, R. P.: Eczemas of Bread Bakers and Confectioners, Brit. J. Dermat. **37**:163 (April) 1925.

3. DeJong, O.: Suggested Aetiology of Bakers' Dermatitis, Lancet **1**:894 (May 5) 1923.

4. Tankard, A. R.: Bakers' Eczema, Lancet **2**:279 (Aug. 11) 1923.

5. Mummery, N. H.: Bakers' Dermatitis, Lancet **2**:647 (Sept. 26) 1925.

refuted by Parsons,[6] with the remark that there is not any appreciable increase in this disorder, and that many cases of scabies and other infections and dermatitides are erroneously diagnosed as "bakers' itch."

Similar problems are presented in many other trades and industries, but the citing of this one should serve to indicate opportunities and needs for investigation.

Excepting Percival Pott's work on "chimney sweeper's cancer" in 1775, little has been written on occupational dermatoses by the English until Robert Willan referred to the psoriasis diffusa of bakers, the psoriasis palmaris of shoemakers, the grocers' itch, the washerwomen's eczema and the dermatoses of metal workers. In recent years, valuable contributions have been made, in particular by Prosser White, and also by O'Donovan,[7] Gardiner[8] and others. Early in the nineteenth century, Alibert wrote what was probably the first French article on occupational dermatoses, and this was followed by papers from Gibert, Devergie and others. The Germans entered the field late in 1842, with an article by Cless, but have since made the most exhaustive studies. The monographs collected by Ullmann, Oppenheim, and Rille are probably the most notable contributions to this subject in any language.[9]

The study of occupational dermatoses in this country may properly be considered as having begun with a presentation by Dr. James C. White before the American Dermatological Association in 1896. In a paper entitled "Notes on Dermatitis Venenata,"[10] he called attention to the need of investigating carefully all cases of this disorder for etiology, especially in "the arts". Other American contributions written within the last fifteen years are those of Schamberg,[11] Fordyce,[12] Knowles,[13] Hazen,[14] C. J. White,[15] Alderson,[16] Pusey,[17] Lane,[18] Stokes,[19]

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6. Parsons, A. C.: Abstract of Report on Bakers' Itch, J. Indust. Hyg. **5**:410 (March) 1924.

7. O'Donovan, W. J.: Brit. M. J. **2**:499 (Sept. 16) 1922; Brit. J. Dermat. **33**:291, 1921; **36**:477, 1924; Lancet **1**:570, 1922; **2**:597, 1925; **1**:599, 1925; **2**:617, 1925.

8. Gardiner: Brit. M. J. **10**:1263, 1908; Brit. J. Dermat. **34**:297 (Oct.) 1922.

9. Ullmann, Oppenheim and Rille (footnote 1).

10. White, J. C.: Boston M. & S. J. **136**:77, 1897.

11. Schamberg: J. Cutan. Dis. **28**:644, 1910.

12. Fordyce, J. A.: Occupational Skin Diseases, J. A. M. A. **59**:2043 (Dec. 7) 1912.

13. Knowles, F. C.: Eczema, J. A. M. A. **68**:79 (Jan. 13) 1917; Bakers' Yeast, ibid. **69**:1234 (Oct. 13) 1917; J. Cutan. Dis. **31**:11, 1913.

14. Hazen: J. Cutan. Dis. **32**:487, 1914.

15. White, C. J.: Skin Diseases, Boston M. & S. J. **175**:35 (July) 1916.

16. Alderson: Cutaneous Medicine, J. A. M. A. **70**:71 (Jan. 12) 1918.

17. Pusey, W. A.: Industrial Dermatoses, Their Sources, Types and Control, J. Indust. Hyg. **1**:385 (Dec.) 1919.

Cole and Driver,[20] E. L. Oliver,[21] L. Oliver,[22] Ravogli,[23] Page,[24] McCord,[25] and others.

To quote White:[26]

> The relative incidence of occupational diseases of the skin and the types met with in different countries and districts depend upon the special genius of the people and the industrial resources of the locality. The nations which have been foremost in the industrial and chemical renaissance of the last few decades, notably France, Germany, England and America, have produced most of the medical literature on this subject.

INCIDENCE

The incidence of industrial skin diseases varies with the locality in which the observations are made and with the social status of the group from which deductions are drawn. Statistics are therefore relative and variable, and their value is dependent on the interpretation made.

The percentages of occupational dermatosis among all skin cases observed were reported as 2 by Fordyce,[12] 10 by Guy Lane,[18] 16 by Knowles,[13] 20 by Oppenheim,[27] 20 by Hazen,[14] and 25 by White.[26] Occupational dermatitides comprised 5 per cent of 37,000 cases reviewed by Knowles, 8 per cent of the inflammatory dermatoses recorded by Oppenheim and 72 per cent of Gardiner's [8] group of 12,000 dermatitides. R. P. White [26] estimated the new dermatologic cases in England as about 300,000 annually, exclusive of burns, scalds, septic sores and

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18. Lane, C. G.: Occupational Dermatitis in Dentists. Susceptibility to Procain, Arch. Dermat. & Syph. **3**:235 (March) 1921; Industrial Dermatitis at Massachusetts General Hospital, ibid. **6**:665 (Nov.) 1922; Essential Factors in Recording Skin Diseases Due to Occupation, J. Indust. Hyg. **5**:366 (Feb. 24) 1924; Skin Diseases with Particular Reference to Their Industrial Application, ibid. **7**:445, 1925.

19. Stokes, J. H., and Brehmer, H. E.: Syphilis in Railroad Employees, J. Indust. Hyg. **1**:419 (Jan.) 1920.

20. Cole, H. N., and Driver, J. R.: Industrial Dermatoses, J. Indust. Hyg. **4**:425 (Feb.) 1923.

21. Oliver, E. L.: J. Indust. Hyg. **1**:246, 1920.

22. Oliver, L.: Skin Diseases Commonly Seen by Industrial Physicians, J. Indust. Hyg. **4**:21 (May) 1922.

23. Ravogli, in Ullmann, Oppenheim, and Rille: Die Schaedigungen der Haut durch Beruf und gewerbliche Arbeit, 1922, vol. 1, p. 296.

24. Page, C. G., and Bushnell, L. D.: Oil Folliculitis, J. Indust. Hyg. **3**:62 (June) 1921.

25. McCord, C. P., and Kilker, C. H.: Zinc Chloride Poisoning, J. A. M. A. **76**:442 (Feb. 12) 1921. McCord, C. P.; Kilker, C. H., and Minster, D. K.: Pyrethrum Dermatitis, J. A. M. A. **77**:448 (Aug. 6) 1921.

26. White, R. P.: Occupational Affections of the Skin, ed. 2, New York, Paul B. Hoeber, 1920.

27. Ullmann, Oppenheim, and Rille (footnote 1, third reference).

other lesions, and he considers about 25,000 of them occupational dermatitides. C. J. White [15] recorded 120 trades and occupations as productive of skin disorders, though the actual number is greater and is constantly increasing. In a single industry, tanning, Minster [28] recorded 42 occupational hazards, of which more than 26 were of a dermatologic nature.

In new industries, the disease and incidence of disability are always higher before protective and regulatory measures have been established and apparently before tolerance has been acquired by the workers. Among 2,000 laborers in oils and lubricating compounds, McConnell [29] observed 25 per cent who developed skin disorders, but this incidence was reduced to a negligible figure by improved hygiene. McCord [25] found that 30 per cent of the employees of an insect powder factory had been subject to industrial dermatitis of variable degree, while preventive measures were not in force. Shufflebotham [30] observed fourteen cases of aniline poisoning in an organization with thirty employees, but later recorded an absence of any serious cases after one year of preventive measures.

ECONOMIC AND LEGISLATIVE CONSIDERATIONS

The growth of industry has resulted in much trade specialization, introducing new industrial diseases and serving to increase the total of such disorders. The growth in particular of chemistry in industry has increased tremendously the liability to occupational dermatoses. Trade specialization, at the same time, has made it difficult for the person with an occupational skin disease to change to work which would be less hazardous to him. He has learned to do a certain type of work, and he is not useful to his employer or to others at any other job. Improved working conditions, however, in modern factories, with shorter hours and higher wages and the consequent higher standards of living among the working people, have undoubtedly reduced the incidence of industrial disease in the United States.

The widespread introduction of workmen's compensation legislation has developed industrial insurance and has resulted in the introduction and maintenance of first aid departments and medical service by most large industrial concerns or their allied insurance companies. Most occupational diseases and injuries, including those of the skin, are cared for by the industrial surgeon, and frequently only those conditions presenting special problems of diagnosis, therapy and prognosis are referred to the specialist. The dermatologist, called on to assume

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28. Minster, D. K.: Forty-Two Occupational Disease Hazards in One Industry, J. Indust. Hyg. **7**:299 (July) 1925.

29. McConnell, W. J.: Industrial Dermatosis Among Printers, U. S. Pub. Health. Rep. **36**:979 (May) 1921.

30. Shufflebotham: Brit. M. J. **2**:490, 1908.

the rôle of medical expert and referee, must therefore possess a thorough knowledge of this particular phase of his subject and judicial ability in the interpretation of cases.

Twelve years before this article was written, the state of Wisconsin established an industrial commission to which the worker may appeal for real or fancied grievances growing out of alleged industrial injury or disease. This service costs him nothing for a fair and impartial consideration of his case, though he may engage a lawyer or a physician, and he may appeal to the supreme court in the event of an adverse decision. Other states have established similar commissions.

The tendency of such commissions, and notably of juries, to favor the workman has made difficult the evasion of responsibility for industrial disease and has increased the demand for the medical specialist in the diagnosis and treatment of these conditions and for medicolegal aid.

Pusey [17] remarked that experts in industrial medicine are not experienced in dermatology, and that the dermatologists have not given systematic study to occupational diseases. Lane [18] believed that the diagnosis and treatment of industrial dermatoses should be carried out by the dermatologist, whereas their cause and prevention are within the province of the industrial physician. It is my belief that the treatment of all industrial skin disorders can be most expeditiously managed or directed from their incipiency by the dermatologist, and that a manifestation of active interest in this field by the dermatologist should result in a widening of his sphere of influence to the benefit of industry.

TERMINOLOGY

The general adoption by clinics, hospitals and individual physicians of a uniform classification of occupational skin disorders, such as that proposed by Lane,[31] would do much toward the development of this subject by simplifying and enhancing its study and by increasing the accuracy and value of statistical investigations. Lane proposed the term "dermatosis industrialis" for all pathologic skin diseases of vocational origin, to be supplemented by the qualifying suffix, "venenata", "eczema" and similar terms descriptive of the clinical pathology of the process, and an additional etiologic or occupational designation. Thus a certain "trade eczema" would be classified as "dermatosis industrialis, eczema, baker" and an oil acne as "dermatosis industrialis, folliculitis, oil." In addition to this, greater accuracy than is commonly employed in the keeping of records must be initiated. The exact nature of the work at which a dermatosis developed, the length of

31. Lane, C. G.: Classification of Industrial Skin Diseases, Arch. Dermat. & Syph. **7**:77 (Jan.) 1923.

time spent by the patient at that work and the exact nature of the irritant, if known, should be recorded with information as to duration of the disease, disability, previous cutaneous disorders, other illnesses and so on. Every patient entering the clinic for skin diseases of the London Hospital is questioned in detail regarding the exact nature of his employment and of the materials handled, and in certain cases the employer is consulted for particular information.[7]

The classification of inflammatory dermatoses, which constitute the largest and most important group of industrial dermatoses, necessitates recognition of the time-honored academic dispute over eczema and dermatitis. I would consider eczema a dermatitis occurring in an allergic or specially sensitized skin and would differentiate between occupational dermatitis and occupational eczema on a basis of differences of degree in manner of reaction, extent of eruption, chronicity and tendency to relapses, as related to the presence or absence of an allergic state.

While not simplifying classification, Oppenheim's [27] differentiation of the inflammatory dermatoses is helpful in their interpretation. He recognized three chief types—the "toxicodermias", "circumscribed occupational dermatitis" and "occupational eczema"—which represent reactions to irritation in idiosyncrasic, normal and allergic skins.

He defines the toxicodermic type as an erythematous, edematous or exudative inflammation of sudden onset and of considerable intensity, following minimal irritation, with a tendency to progression even after removal of the irritating agent. The condition is ascribed to an idiosyncrasy to the particular irritant and its occurrence is comparatively infrequent.

Circumscribed occupational dermatitis usually develops in a skin that gives normal reactions, after prolonged or intensive exposure to a pronounced irritant, though its development may be attributed in part to a temporary hypersensitiveness of the skin or to an increase in the strength or activity of the irritant. It appears to me that this point is illustrated by Wayson's [32] report of dermatitis as it occurs in the Hawaiian pineapple canning industry. The cans are passed through hot baths of Japanese lacquer *(Rhus vernicifera)* and gasoline, and many of the workers, especially the elderly ones, develop dermatitis. Those handling cold cans are subject to a mild dermatitis of a few days' duration, while those who handle hot cans, in which the irritant presumably is more active, are more liable to develop a severe dermatitis which manifests itself as a typical *Rhus venenata* eruption of pronounced intensity and runs a course of two weeks or longer. The

32. Wayson: Lacquer Dermatosis or Dermatosis Industrialis, Arch. Dermat. & Syph. **8**:77 (July) 1923.

circumscribed dermatitis usually embraces erythematous, vesicular and exudative inflammation in varying combinations, which remains fairly localized to the area of contact with the irritant and subsides shortly after removal of the irritant without tendency to spread. This condition is comparatively common, and the dermatitis venenata of surgeons and nurses may be cited as examples of it.

Artificial or occupational eczema, similar at its onset to the second group, develops in a sensitized skin following irritation of variable intensity, tends to spread peripherally, progresses even after removal of the irritant, and shows involvement of new areas from time to time with inclusion of parts distant from the original site of irritation. It shows a tendency to exacerbations and chronicity rather than a tendency to healing. This type of dermatitis implies associated anaphylactic or allergic conditions and its comparative frequency, and as it is the most common of the three types described, it suggests the frequency of allergy. Oppenheim stated that a toxicoderma or a dermatitis may sensitize the skin so that an eczema develops before the preceding condition has disappeared.

ETIOLOGY

A proper interpretation of the etiology of the occupational dermatoses presupposes an understanding of the underlying physiologic and pathologic principles. Blaschko [33] has inquired into this phase of the subject. He states that, while some occupational dermatoses may be considered as partly of internal origin, the great majority are a result of external irritation, and the dermatosis in a given case is the product of an external action specifically related to the work performed and a cutaneous reaction. A dermatosis develops only if the intensity of the irritation suddenly passes the limit or threshold of tolerance or if the injury is of too long duration, in either of which instances the cutaneous reaction passes physiologic limits and becomes pathologic. Normal tolerance and power of adaptation protect most persons from the development of occupational dermatoses. The one who develops a dermatosis or injury may have a lower threshold of tolerance, in which case he is hypersensitive.

Blaschko considers that in an affected person there is not only a hypersensitiveness of the local tissue, but also a pathologic manner of reaction. The latter may be inherent or hereditary, or it may be acquired; it may also be overcome by adaptation. A variation in the manner of reaction may be occasioned by a disturbance of circulatory, nervous, visceral or trophic nature, induced by tissue peculiarities or

33. Blaschko, in Ullmann, Oppenheim, and Rille (footnote 1, first reference, p. 1).

by constitutional disease. Jadassohn recognizes a general susceptibility which renders the skin sensitive to all forms of irritation and a special susceptibility which is confined to certain irritants.

Local tissue hypersensitiveness is a predisposing cause and may be considered physiologic in youthful, senile, female and blond skins, and pathologic in excessively dry or abnormally moist skins and in persons previously injured, in those affected by disease or those sensitized by repeated exposures to irritants. One of the greatest predisposing factors to occupational dermatitis is water; another is uncleanliness, though dirt in itself is not often a factor and the so-called dirty occupations are remarkably free from cases of occupational dermatoses. Water predisposes to dermatitis indirectly as a vehicle by favoring closer contact of the skin with bacteria, parasites and fungi, as a solvent for irritating chemicals, such as dyes, soaps, acids and alkalis, and directly as an irritant by lowering the resistance of the skin to other irritants and infectious agents through removal of protective natural oil and by causing a softening and swelling of the epidermal cells.[34]

General predisposing factors include the sensitization caused by allergic or anaphylactic conditions caused by foods and other agents, toxins, focal infections and constitutional disorders and unfavorable and unhygienic conditions in the home and at work. In a study of several hundred cases of inflammatory occupational dermatoses, Gardiner [8] observed that one seventh of the patients gave histories of definite preceding illness, and almost two-thirds showed evidence of preceding cutaneous abnormalities, such as ichthyosis, hyperhidrosis, seborrhea and various cutaneous inflammations. Jacquet and Jourdanet [35] claimed that by correcting faulty habits of eating, a large percentage of occupational dermatitides can be cleared up without recourse to local treatment.

EXCITING CAUSES

Since it is acknowledged that injury or insult of the tissue is usually prerequisite to the development of an occupational dermatosis, a consideration of the types of these exciting causes is in order. These may be grouped as physical, chemical and infectious.

Physical injuries result from mechanical, thermal and actinic agencies.

Mechanical injuries result from pressure, traction, friction or compression carried beyond the point of tissue tolerance, which is considerable because of the peculiar anatomic structure of the skin. These

34. Glaser, in Ullmann, Oppenheim, and Rille (footnote 1, third reference, p. 51).

35. Jacquet and Jourdanet: Ann. de dermat. et syph. **2**:12, 1911.

injuries are common in so-called "rough occupations," and, while they result chiefly in industrial accidents of the surgical type, such as lacerations, puncture wounds and cuts, they also result in occupational dermatoses, such as excessive callous formations which cause functional impairment or disability, and in inflammatory dermatoses due to friction; they also predispose to secondary chemical and infectious dermatoses because of the impairment of the normal cutaneous defense.

Thermal injuries result from direct contact with destructive heat, as in burns and scalds, from direct action of radiant heat, as in the erythema ab igne of metal pourers, bakers, cooks and stokers, and indirectly by the production of miliaria and the activation of inflammatory dermatoses, such as seborrheic dermatitis, caused by heat and perspiration. Hydrocystoma, due to heat and moisture, has been referred to by Fordyce [12] as an occupational development in laundresses. Among thermal injuries should be included the large number of electrical injuries due to accidental exposure to electric currents. Thermal injuries due to cold, as frostbites and chilblains, are peculiar to certain outdoor workers, such as teamsters, cab drivers, mail carriers, farmers, cold storage workers and florists. A predisposition to these forms of injury is occasioned by the vasodilation of exposed areas in workers of this type, while an increased range of tolerance to heat or cold may be racial or the result of adaptation. Negroes tolerate extreme heat with less liability to skin injury, and northern races withstand extreme cold.

Actinic agencies produce cutaneous changes peculiar to farmers, sailors and other outdoor workers, predispose to diseases like lupus erythematosus and are responsible for certain industrial injuries such as those seen in photo-electric workers and in metal pourers. Injuries in physicians, nurses and technicians caused by the roentgen ray and radium come in this category as do necroses of the bone occurring in workers with radium-luminous paint. Castle and Drinker [36] considered the latter condition a result of the inhalation of particulate matter containing a radium salt which is subsequently deposited in the bone, and drew an analogy between this condition and necrosis of the bone observed in phosphorus poisoning.

Malignancies, in addition to those following injuries from radium and the roentgen ray, may result from arsenic, tar and soot, and may occur secondarily to physical injuries. In regard to the latter, it should be recorded that malignancies resulting from occupational injury are not commonly considered occupational except when prolonged occupa-

36. Castle, W. B., and Drinker, K. R.: Necrosis of Jaw in Workers Employed in Applying Luminous Paint Containing Radium, J. Indust. Hyg. **7**:371 (Aug.) 1925.

tional contact with a known provocative agent is evident. Chimney-sweeps, mule-spinners and workers in pitch, shale oil, paraffin, tar, petroleum, aniline, asphalt, anthracene and arsenic are peculiarly liable to carcinoma. O'Donovan [37] and Legge each observed three cases of arsenical carcinoma within a comparatively short time in a small manufacturing center of London. Pronounced hyperkeratosis due to continued irritation, terminating in carcinoma, was considered occupational by O'Donovan [38] in the case of a workman who developed carcinoma of the thumb following the use of a hot poker for ten years.

Injuries of chemical origin comprise probably the largest group of industrial dermatoses, particularly the inflammatory dermatoses, and result chiefly from coal tar derivatives, acids, alkalis and plant and wood poisoning. An intact epidermis is the chief defense against chemical injuries; the follicles and ducts of the skin are the vulnerable points in which chemical dermatoses frequently have their origin. Chemical agents produce tanning, cauterization and swelling of the epidermis and also act by removing the natural protective oily covering and by macerating the epidermal cells. These actions produce dryness, loss of elasticity, fissuring and denudation, and thus permit the penetration of chemicals and lead to dermatitis, ulceration, necrosis and subsequent secondary infection with the normal bacterial flora of the skin or with extraneous organisms. Many organic and practically all inorganic chemicals produce skin injuries of variable intensity in susceptible persons; enumeration, therefore, is hardly necessary. Of these, the alkali soaps, because of their extensive use, are responsible for the largest number of occupational dermatoses resulting from a single agent.

Infectious agents as causes of industrial dermatoses include animal parasites, bacteria, fungi and protozoa. Many of these infections are secondary, if one assumes the occurrence of mechanical or chemical injury as a precursor which breaks down the normal defense.

Animal parasitic diseases include pediculosis and scabies and are occupational hazards when large groups of persons are congregated, as in armies and in work camps and on work trains. These conditions are frequently complicated by disability, and produce bacterial infections of the impetiginous and ecthymatiform types. Pusey [17] states that during the last war such conditions in the trenches produced the greatest amount of disability occasioned by disease. "Grain or straw itch", due to the pediculoides ventricosus has been referred to by Schamberg and Michelson and Legge [39] as an occupational hazard in

37. O'Donovan (footnote 7, second reference).

38. O'Donovan (footnote 7, first reference).

39. Legge, R. T.: Industrial Medicine, California State J. Med. **19**:464 (Feb.) 1921.

farmers, packers handling straw, and millers. "Ground itch", or uncinariasis, causes a dermatitis which occasionally may be occupational in origin. Horticulturalists and entomologists are liable to dermatoses from caterpillars, moths and insects. Copra itch, due to a mite similar to *Acarus scabeii,* has been observed in workers in the copra mills.[40]

Infections of bacterial origin form the largest and most important of this group and are chiefly staphylococcic. The pustular folliculitis and furunculosis in industries in which oils and greases, paraffin, and tar are used produce a large amount of disability. In such cases these materials favor infection by plugging the follicles and ducts and by causing dermatitis. In industries in which "cutting oils" are used, infection results chiefly because of mechanical injury with sharp particles of metal in the oil. Bacteria normally present on the skin or subsequently introduced on vulnerable tissue are responsible for the eczematization of many chemical dermatitides complicating the diagnosis and prolonging the disability. Direct bacterial infections in industry include the erysipeloid of butchers, farmers and fishermen; anthrax in workers with wool and hides; vaccinia in milkers; foot and mouth disease and glanders in farmers, cattle dealers and grooms, and the cutaneous tuberculosis of butchers, cooks and undertakers.

Infections of fungus origin as primary occupational conditions include the trichophytosis observed in farmers, horse and cattle dealers, and handlers of fresh hides, sporotrichosis as seen in horticulturalists and farmers,[41] blastomycosis and actinomycosis in farmers, the mycotic paronychia and dermatitis of fruit canners described by Kingery and Thienes [42] and many cases of epidermophytosis. Secondary infections of occupational dermatitides, especially with the epidermophyton fungus, are of importance.

Protozoan infections include the syphilis insontium of nurses, physicians and midwives, and some cases of malaria and yellow fever in workers in tropical zones. Syphilis, not occupational in origin, has been incriminated by Oliver [21] and by Alderson [16] as a factor in reducing industrial efficiency and in retarding recovery from industrial injuries or disease. Stokes [19] has directed attention to the unrecognized menace of this disease in railroad employees, both as regards the personal welfare and industrial efficiency of the employee and the safety of the traveling public. Among more than 1,000 cases, Stokes found syphilis eight times as prevalent among railroad men as among farmers,

40. Hirst and Castellani: Brit. J. Dermat. **25**:21, 1913.

41. Foerster, H. R.: Sporotrichosis, an Occupational Dermatosis, J. A. M. A. **87**:1605, (Nov. 13) 1926.

42. Kingery, L. B., and Thienes, C. H.: Mycotic Paronychia and Dermatitis, Arch. Dermat. & Syph. **11**:186 (Feb.) 1925.

three times as prevalent as among tradesmen and twice as prevalent as among common laborers. Of the fifty men studied by Stokes, 76 per cent were engaged in the actual operation of trains and of thirty-nine adequately examined, 80 per cent had syphilis of the nervous system, 38 per cent of whom showed mental symptoms.

CLINICAL PATHOLOGY

As a generalization, it may be said that there is no specificity as regards the clinical manifestations of occupational dermatoses, that a variety of manifestations may be produced by a single irritant, and that different irritants may produce lesions clinically identical.

Lesions may develop immediately after contact, as in insect bites, in some plant irritations and in certain mechanical and electrical injuries; or in from several hours to several days or even weeks and months following organic and inorganic chemical irritants, and years later in roentgen-ray injuries and in cases of arsenical or tar carcinomas. Irritants that act on the skin in the form of dust or vapor have a more rapid effect than those of liquid or solid form. Most cases of industrial dermatitis occur within the first few weeks following employment of the type causing the dermatitis or not until after a number of years of such employment. Alterations in strength or composition of the materials used may precipitate attacks of dermatitis in persons previously unaffected. Industrial dermatoses are usually localized to the area or areas of injury, and in the dermatitides the inflammation usually involves the hands and forearms and the face and neck, though any or all regions may be involved. In toxic inflammations the areas of involvement are usually the areas of contact, the extensor surfaces of the extremities, the face, the neck, the genitalia and the areas of opposing skin surfaces. Inflammatory occupational dermatoses exhibit the same primary and secondary lesions of inflammation characteristic of non-occupational dermatitides, and their differentiation is therefore frequently difficult. Some irritants at times produce characteristic eruptions, of which a few may be mentioned. Scarlatiniform eruptions have been observed following contact with mercury, phenol, arsenic, turpentine and satin wood; morbilliform eruptions have been noted following irritations with ethereal and balsamic oils and certain dry plant products; meshlike erythemas and pellagra-like eruptions have preceded war melanoses, and acute diffuse erythemas have been seen following illuminating gas poisoning. Erysipeloid erythema occurs in the primula dermatitis of florists and in satin wood and ivy poisoning. Purpuric lesions have been observed following absorption of quinine, chrome, and benzene, and in caisson disease.

Oppenheim [43] considered that every trade or occupation eventually leaves its mark on the skin. These stigmas occur in all persons with definite regularity, though in variable intensity, following pursuit of a particular occupation for a length of time. Manual workers show changes of the hands with peculiarities indicative of certain types of work.

DIAGNOSIS

The diagnosis of industrial dermatoses is usually obvious, being indicated by the localization and character of the skin injury and its associated history. It is, however, often arrived at only by a process of careful elimination, and in this particular, a knowledge of dermatology is essential. Most difficulties arise with inflammatory dermatoses of the venenata and eczematoid types in which a careful investigation of the predisposing as well as of the exciting factors is necessary for the establishment of the status of a given case. There are numerous infections due to pathogenic organisms and to organisms not previously pathogenic, occurring secondarily through occupational activity or disease. These conditions, superimposed on involuting occupational dermatitides, usually show the clinical characteristics of the infectious agents. An example of this type is the dermatitis caused by the ringworm fungus. Another condition frequently observed is an infectious eczematoid dermatitis developing into a disabling condition from a minor localized dermatitis of occupational origin. It is necessary to be on the alert constantly for an industrial origin in cases of dermatitis of the hands and face.

INTERPRETATION OF STATUS OF CASES

A nonoccupational disorder, such as a localized patch of eczema in a seborrheic person, becoming activated through neglect or injudicious treatment and possible associated unhygienic surroundings at work, or through excessive perspiration at work, and developing into a disabling generalized infectious eczematoid dermatitis, should not, I believe, be considered a compensable condition. If, however, the same person, with a latent or active seborrheic dermatitis, develops a dermatitis in line with his work as a result of contact of his pathologic skin with chemical or other irritants peculiar to that occupation, or as a result of injury at work, I would consider the resulting condition an occupational disease, even though it may be argued that the previously existing nonoccupational dermatitis was a necessary predisposing factor. According to legal interpretation,[44] compensation is not depen-

43. Oppenheim in Ullmann, Oppenheim and Rille (footnote 1, first reference, p. 38).

44. Design of Compensation Act, Aggravation of Syphilis, Medicolegal, J. A. M. A. **88**:593 (Feb. 19) 1927.

dent on any implied assumption of perfect health and does not exclude the weak or physically unfortunate or those with latent and unknown tendencies to disease. The employment of a man is in itself an assumption that he is physically and mentally fit for the work.

Another consideration is that of a secondary dermatitis, as for example an epidermophytosis, developing on an occupational dermatosis. Even though it can be proved to be an *Epidermophyton* infection, I should under those circumstances consider the condition compensable, for the occupational disorder was a direct predisposing cause of the infection. If, however, an epidermophytosis develops, or a latent infection of this type becomes activated, possibly through excessive perspiration or warmth at work, without an immediately preceding and existing occupational injury or inflammation, the disease should not be considered as compensable, because it would not have been a direct consequence of occupation. A similar interpretation applies to furunculosis as originating in an industrial oil or tar folliculitis and furunculosis occurring incidentally without such occupational relationship.

If a person develops an ulcerating syphilid at the site of an industrial injury, the employer may be considered liable for treatment necessary to heal the injury and the localized syphilid, but he is not liable for further antisyphilitic treatment.

The interpretation of the status of liability in such cases, and in many similar ones, is a perplexing one of considerable economic importance because of the frequency with which it arises. A thorough knowledge of the differential diagnosis of skin diseases should be a necessary qualification for such work. The interpretation made by the dermatologist is almost always accepted by the insurance company or employer. The responsibility placed on a dermatologist therefore necessitates a most careful study of the case, a deliberate unbiased consideration of all the facts at hand and an exhibition of sound common sense in arriving at conclusions. Above all, the physician should not attempt to make a medicolegal analysis the basis of his opinion and should not indulge in hypothetic speculation.

Malingering in industrial dermatoses is of special importance. While there are occasional instances of primarily self inflicted skin injuries and dermatoses, most cases of malingering in my experience have had their origin in bona fide dermatoses in which healing was interfered with by the patient to prolong disability under pay or to gain an increase in compensation. The detection of factitious skin lesions is especially difficult for the physician without dermatologic training and experience, and errors of diagnosis in such cases are of special importance because of monetary interests.

PREVENTION AND TREATMENT

The treatment of industrial dermatoses is largely a matter of adequate prophylaxis and appropriate immediate treatment. The large sums spent on compensation for disability have emphasized the hazards of disease or injury, more particularly in certain industries and have forced the introduction of protective devices and prophylactic measures Prophylaxis necessitates improved working conditions, medical inspection, and education of the employee in personal hygiene. The modern factory, with its adequate provision for ample working space, sunlight, fresh air, proper washing and toilet facilities and short hours is a boon to the workman, whereas unhygienic working conditions are often directly responsible for a high incidence of industrial disease. The replacement of methods of work which necessitated direct contact of the hands with irritant materials by mechanical methods of manipulation and manufacture, brought on by large scale production, is an advance in prophylaxis.

In some industries a frequent thorough cleansing with soap and water is advised, and in some factories it is made compulsory. Bathing facilities are provided, and bathing is encouraged by including it in the working schedule. The frequent changing of dust-laden and oil-soaked clothing is as important as washing. In particularly hazardous work, the temporary shifting of workmen to other jobs should be a routine measure.

A reduction of dermatitis among printers has been noted by McConnel [29] following applications of hydrous wool fat to the hands and arms before work and cleansing with a mixture of saw-dust, green soap and water. In the wood preservation industry, in which poisoning by zinc chloride is frequent, the workers' hands are protected with flexible "linoleated" canvas gauntlets and zinc burns are promptly neutralized with sodium bicarbonate.[25]

The use of paint solvents for cleansing is discouraged by Turner,[45] who believes that most inflammatory dermatoses among painters are a result of the irritation, drying out and subsequent dermatitis occasioned by the use of turpentine and benzine. Turpentine dermatitis is especially apt to follow the use of artificial or wood-distilled turpentine. Page and Bushnell [24] considered the most effective prevention of dermatitis and folliculitis from oil and grease to be cleanliness on the part of the worker and the avoidance of a promiscuous interchange of waste and rags used for wiping the hands. They consider that daily filtration and sterilization of used oil are helpful, the addition of germicides useless and the removal of workers with skin diseases the most important factor in prophylaxis.

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45. Turner, J. A.: Mycotic Paronchyia and Dermatitis, J. Indust. Hyg. **7**:293 (July) 1925.

Preventive measures should be directed by experts familiar with factory technic, management and medical administration, and require accurate knowledge of working conditions and materials handled, the risks involved and the exact causes of industrial disease.

Routine medical inspection of applicants and employees should permit, to some extent, the elimination of those physically unfit for particular types of work, and the building up of an immune or resistant personnel, and should result in the early detection and treatment of predisposing and exciting factors. Persons with hyperhidrosis, seborrhea, and xeroderma, and those with active cutaneous disease or history of such disease should be eliminated from industries in which the liability to dermatoses is high. Evidence of impaired health, as an indication of predisposition to injury or disease, should receive attention, and workers showing intolerance to work or materials should be removed from such work at the first onset of symptoms.

In all industries, compulsory immediate notification concerning minor injuries and eruptions, by permitting appropriate first aid treatment, will do much toward the elimination of disabling infections and dermatoses. Roller towels and common drinking cups should be prohibited. Bland protective ointments, gloves and other protective measures during work, and germicidal and neutralizing solutions after work, should be employed as a routine when their value has been proved.

The active treatment of industrial dermatoses is the treatment of the clinical conditions present, the removal of the etiologic factors and the institution of protective or preventive measures following recovery. It requires the same consideration of the patient's general health and symptomatology as does the treatment of nonoccupational dermatoses. The first treatment is the most important, and this assumes correct diagnosis. It is a frequent observation that the use of strong ointments and germicides as first aid measures and injudicious home or factory treatment are important factors in the intensification and extension of a dermatitis and in the prolongation of disabilities. The management of dermatoses at their incipiency by the dermatologist is therefore a measure of economy.

A workman developing a dermatosis should either be taken from work immediately or be kept under close observation while at work. A new man should preferably not be reemployed in the same industry, whereas an old and skilled employee, after recovery from a dermatitis should temporarily be placed at other work sufficiently long to permit the disappearance of the temporarily heightened susceptibility to irritation. Before a patient is discharged from treatment the last vestiges of a dermatitis should be eliminated, for residual disease is usually responsible for recurrences.

CONCLUSION

Advances in industrial medicine are to be expected from the establishment of industrial clinics, like those of the Massachusetts General Hospital and the Institute Obrech for Occupational Diseases in Moscow. The latter is a hospital and dispensary with seventy-five beds and five laboratories, employs sixteen physicians for the treatment and special study of industrial disease, and maintains a "Museum of Safety" for instruction in trade dangers and precautions.[46]

Laws in the interest of the workman suffering from industrial disease have existed in England for more than fifty years, have more recently been introduced into the United States and are increasing in number, scope and power in all countries. The subject of industrial disease in this country, as elsewhere, is being given increasing attention and more intensive study, and it is important that the dermatologist, by reason of his specialized training and knowledge, shall take a prominent part in the further development of this field of medicine.

ABSTRACT OF DISCUSSION

DR. JOHN H. STOKES, Philadelphia: The summary that Dr. Foerster has given should be brought to the attention of every industrial physician in the country. I wish to emphasize one point which he, because of lack of time, did not stress as hard as he otherwise would have, and that is the need for careful inspection of men with cutaneous diseases who may act as carriers of infections. The most striking example I ever saw of this was during an epidemic of furunculosis; sixteen cases which occurred in a nickel plating room caused that part of the plant to be closed for some time. It was due to the admission to the workroom of one man with a small furuncle on his hand. The emphasis that should be laid on the need of careful cutaneous inspection cannot be too great in reference to carriers of infection.

DR. C. GUY LANE, Boston: Dr. Foerster has given an excellent demonstration of the industrial dermatosis situation. I believe in emphasizing the classification he has given. A great deal of work has been done on this subject in England, and I think it well worth while to emphasize in this country the position in which these cases should be placed. The more one looks for these cases, the more one sees the two types Dr. Foerster has spoken of, those which are undoubtedly industrial conditions and the nonoccupational cases which are undoubtedly influenced by the work the patient is doing. In some states, the latter cases are legally considered as entitling the patient to compensation and in other states they are not. I think these cases should be classed as industrial cases if they are unfavorably influenced by the work the person is doing.

One cannot stress too much the need for careful inspection of the history in these cases, particularly the obtaining of an accurate history of the industrial aspects. One should know the details of the onset of the trouble, the relation of it to the patient's job, the exact type of work being done and other particulars. It is only by such a history and a careful study that it is possible to classify these cases as accurately as some of the industrial physicians in England do.

In making a diagnosis, it has been my habit to place these cases in four groups. The first group is that in which one is practically certain that the cases are industrial. The next group is that in which there is not quite as much evidence, but which one can say are "probably industrial." The third group con-

46. Hamilton and Hills: J. Indust. Hyg. **7**:47, 1925.

tains those in which there is less evidence, and one can say that they are "possibly industrial," and, finally, the group which is nonindustrial. The two middle groups are the ones which require the most careful study in order that at some later time they may be classified either in the first or in the fourth group, for the benefit of the cases which may be encountered later.

In seeing these cases, we are all aware of certain difficulties; first, the lack of industrial knowledge, either a lack of exact knowledge on the part of the patient of the kind of things he is handling, or a lack of knowledge on our part of industrial processes and working conditions. Second, there is the fact that one may see the patient only once. Third, when they may come to us, their lesions may be considerably altered by much previous treatment. Fourth, these patients frequently come for examination a long time after the original condition began, and they have usually forgotten a great many of the necessary facts relating to work, onset, treatment, etc. Fifth, the patients are frequently foreigners, and often the history elicited from poor interpreters is far from accurate.

I believe that these industrial cases are of sufficient economic importance to make it necessary for dermatologists to do all they can to remedy failures in the present situation by watching for such cases and studying them carefully on the basis of a wider knowledge of industrial conditions, a thorough understanding of substances used in various industries, and a more exact knowledge of the effect of industry on diseases which the person already has.

DR. CHARLES J. WHITE, Boston: I wish to speak on one point that Dr. Foerster mentioned in his summary, namely, what is to be done with men who are the victims of dermatitis? We treat them and perhaps cure them temporarily, then they are returned to the same sort of work which sensitized them, and in a few weeks they return to us with exactly the same disease process. I wish that the Association could feel inclined to take some action about regulating the care of industrial diseases. I believe if the insurance companies would spend the same amount of money, or less, in finding other occupations for these victims, the money would be well spent.

DR. E. WOOD RUGGLES, Rochester, N. Y.: I wish to relate an interesting experience regarding a man I first saw in 1923, who had a severe case of chromic acid dermatitis. He worked for a lithographing company, and after this acid had almost ruined his skin he insisted on going back into the same work, being unable to earn as much money elsewhere. He had a more severe attack, and the disorder extended all over his body. It was a long time before the dermatitis finally cleared up. The Utica Mutual Insurance Company paid the first two awards cheerfully. His company then put him in a different department, where he used a great deal of benzene, gasoline and oils, and he suffered from several other attacks. In the meantime, his employers had transferred to another insurance company, and I was called to the stand to testify as to whether this was a continuation of the first liability, or whether the responsibility devolved on the second insurance company. The judge wished me to decide the question as to which company was liable. He seemed unable to grasp the distinction between predisposing and exciting causes. He agreed, however, that the man undoubtedly deserved the compensation.

DR. JOSEPH V. KLAUDER, Philadelphia: An experience in decreasing the incidence of a dermatitis appearing on the hands of workers handling vegetables in the food industry may be of interest. The experience concerns a study of such dermatitis among employees of a well known company that prepares food products. It was observed that the most common vegetables giving rise to dermatitis were tomatoes, carrots, leek and okra, and that it usually appeared not on first contact with these vegetables, but after a period of handling them. We determined the average period elapsing between the first exposure and the occurrence of dermatitis and then rotated the workers just short of this

period to handling other vegetables, for example, from handling carrots to tomatoes, etc. This plan of rotating workers from one vegetable to another greatly decreased the incidence of the vegetable dermatitis. We thought of conducting cutaneous tests on certain employees to ascertain their cutaneous irritability, not only to common irritants such as tincture of iodine, etc., but to idiosyncratic substances to which they were exposed in their particular work. This procedure would determine the type of person who primarily has a heightened irritability as well as those primarily sensitized to many of the idiosyncratic substances used in all industries. I would like to ask Dr. Foerster if he has had any experience in cutaneous testing of this nature.

It may be opportune in this discussion to state that erysipeloid of fishermen, the severe type which Drs. Righter, Harkins and myself have studied and reported, is now being successfully treated with the serum of the bacillus of swine erysipelas. We obtained such an organism from the skin lesions, and it is the cause of the so-called erysipeloid. This infection is the most important disease of the fishing industry. The serum is prepared by Mulford and Company and is injected intramuscularly in an amount as small as 10 cc. This amount promptly cures erysipeloid, which ordinarily runs a course of from three to four weeks.

Dr. Harvey P. Towle, Boston: Industrial dermatoses are a new and interesting phase of dermatology. Because of their clinical symptoms and their etiology, they place on the attendant the double responsibility of being a physician and a judge. He must be able to treat the patient properly for the disease present and to judge whether or not the industry accused is capable of causing the disease. Therefore the judge must inform himself of all the conditions under which the patient has worked. It is absolutely necessary that he should obtain a full and detailed history, not only concerning the onset and course of the disease, but also concerning all the industrial factors. The latter, of course, involves a complete study of the work itself, its methods, its technic and all the environmental conditions. Then with the double understanding of the disease and of the work, we may venture to make the diagnosis of an industrial dermatosis.

Dr. Harry R. Foerster, Milwaukee: With reference to Dr. Klauder's question, it is impossible at this time to carry out routine tests on employees, because industrial concerns do not recognize the necessity for that work. In Milwaukee some of the insurance companies, particularly with reference to dermatoses in the tanning industry, have adopted the routine of caring for the man who develops a dermatitis in that work, treating him until he has recovered, and then advising his employer not to reemploy him.

The question of furunculosis is important in industries in which oils are used, and a great deal of work has been done to determine methods of eliminating dermatoses caused by oil. The most effective method so far has been elimination of the individual contaminant. If the patient is kept from his work from the onset of an infection to its termination, other cases are much less likely to develop.

The interpretation of the law differs in different communities. The worker often obtains a decision in his favor, even when an expert gives an adverse opinion. One reason for this in cases of skin disease is that the dermatologist is often called on to examine or to treat a patient when the condition has existed for a long time, and he therefore cannot always give a positive opinion as to its etiology. Another criticism applies to the fact that the testimony of physicians whom we do not consider competent to diagnose skin disorders or to treat patients for them will sometimes be accepted as a basis for settlement of claims.

ROENTGEN-RAY TREATMENT OF ACNE VULGARIS

END-RESULTS IN ONE HUNDRED AND NINETY-ONE CASES

JEFFREY C. MICHAEL, M.D.
HOUSTON, TEXAS

Every therapeutic measure of value necessarily passes through three stages: evolution, standardization and evaluation. It is discovered or evolved; is used, and by usage becomes definitely formulated; and finally the results obtained, especially the permanent or end-results, are studied and interpreted.

While these periods are not always chronologically distinct, nor always of equal importance, they can be definitely traced in the history of every method of treatment that has passed the twin sentinels of time and trial.

It often happens that methods of therapy have an immediate beneficial influence, even a startling success, but in many cases a follow-up of these seeming cures has shown that the successes are not as uniform as the immediate effect indicated. For this reason, and others which will readily occur, systematic investigation of end-results is desired in any therapeutic measure that has elements of success in it, or that has been fairly well standardized. Occasionally, it leads to improvement in the method by revealing certain hidden but reparable defects. Sometimes the method does not require change, but its application to individual cases becomes better defined.

It seems to me that the roentgen-ray treatment in cases of acne vulgaris, at least in this country, has arrived at the point where its end-results should be studied. Not that everyone employs the roentgen ray in the treatment of this disease, but a great many dermatologists do, and in this country the method advocated by MacKee [1] has, I think, reached a degree of standardization and widespread application that should make a compilation of the end-results obtained by this treatment of interest.

Over a period of five years, from January, 1921, to Dec. 31, 1925, 246 patients with acne vulgaris have been treated by the procedure of MacKee. One hundred and ninety-one of these patients have been traced and the results of the treatment determined. In every case the interval from the last treatment to the time of determination of the

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* Read at the Fiftieth Annual Meeting of the American Dermatological Association, May, 1927.

1. MacKee, G. M.: X-Ray and Radium in the Treatment of Diseases of the Skin, Philadelphia, Lea & Febiger, 1921.

result was at least one year. The patients were first sent a questionnaire; when these were returned, and especially if relapse was reported, a determined effort was made to see them personally, and in at least 60 per cent of both successes and failures a personal interview was obtained. If the patient was not seen, the information as to his or her status was obtained through the patient's answer to the questionnaire or from other sources that were considered reliable.

No record has been included in which the patient did not receive at least ten treatments or a minimum of 2¼ skin units.

While the number of cases left for consideration is not large, I believe that they represent a true picture of the results achieved. The number of cases does not allow definite conclusions, but it at least shows trends which are probably indicative of what a larger compilation would reveal.

METHOD OF TREATMENT

The patients whose cases have been reviewed for this paper have not been treated exclusively by the roentgen ray; they have received in addition to it, dietary regulation and correction of obvious functional and organic disturbances if these were present. Treatment was also given for constipation and menstrual disturbances.

The roentgen-ray treatment consisted of one-quarter skin units, unfiltered, once a week. Every fourth dose was reduced to one-eighth of a unit or omitted and with few exceptions, sixteen weekly treatments (3½ units) were not exceeded. The individual dose was computed by arithmetical computation (Remer and Witherbee); the factors being 2 milliamperes, 6 inch spark gap (sharp point and voltmeter estimation); 8 inch focal point, skin distance, and the time, forty seconds for a quarter unit dose. The same broad focus Coolidge tube has been used for each case. The roentgen-ray equipment is constantly practically checked by its employment in the usual routine of dermatologic practice.

In all other details, the instructions of MacKee[1] were followed implicitly.

The diet given the patients was one restricted as to carbohydrates, with particular emphasis on candy, syrups, pastries, soda water, bread, rice and potatoes. Constipation was combated by a variety of simple measures; including mineral oil, and mineral oil agar mixtures, exercise, and occasionally mild laxatives such as phenolphthalein and cascara. Local applications of a medicinal nature were not permitted while the patient was under roentgen-ray treatment.

LITERATURE

The evolution and application of roentgenotherapy to acne vulgaris originated a voluminous literature which need not be reviewed for this report. It suffices to say that those who have had personal experience of the effect of roentgen ray in acne vulgaris are practically unanimous in giving it first place in the treatment of patients with this disease. Some physicians reserve it for severe cases or for those unresponsive to other measures; many, however, use it as a routine.

The majority of dermatologists of this country, following the plan outlined by MacKee, employ the principles of unfiltered radiation with maximum suberythema skin effect. In foreign countries, or among German dermatologists at least, there seems to be a preference for filtered radiation given in cycles of two or three treatments followed by fairly prolonged periods of rest. The latter method is probably not any more effective therapeutically than the former, but it is claimed to have a greater factor of safety.

Reports on the end-results of roentgen-ray treatment in acne vulgaris are scarce. Hazen and Eichenlaub [2] reported the results obtained in 175 cases in which the patients were treated by a different but comparable dosage to the one employed by me. They state that they "knew of thirty-nine instances in which there was a relapse." Thus the known relapses were approximately 20 per cent. In addition, they mention seven cases in which beneficial effects were not obtained and two others in which there was temporary improvement only. Presumably these were not included in the cases of known relapse, and if included, their failures were increased to 25 per cent.

Crutchfield,[3] who treated his patients strictly according to the method of MacKee, reported 9 per cent of recurrences at the end of the first year following treatment in a series of ninety-six cases. Two thirds of the patients with recurrences responded to further roentgen-ray treatment.

McCafferty and McCarty,[4] following the MacKee procedure, reported a recurrence of 10 per cent in seventy cases. The average age of their patients was 18 years.

MacKee [1] and Remer and Witherbee [5] estimated relapses after roentgenotherapy at about 6 per cent, but this is only an estimate and not an accurate check on the results they obtained. MacKee believed that the regulation of any obvious systemic disturbance and a restricted carbohydrate diet are of value in reducing the number of relapses. The beneficial effect of these adjunct measures are subscribed to by most authors, but Pollitzer [6] does not consider general treatment of any value in acne vulgaris. Some men teach and recently this has been

2. Hazen, H. H., and Eichenlaub, F. J.: Roentgen-Ray Treatment of Acne Vulgaris, Arch. Dermat. & Syph. **4**:671 (Nov.) 1921.

3. Crutchfield, E. D.: Treatment of Acne with X-Ray, Texas State J. Med. **19**:395 (Nov.) 1923.

4. McCafferty, L. K., and McCarthy, C. L.: M. J. & Record **121**:285 (March 4) 1925.

5. Witherbee, W. D., and Remer, John: X-Ray Dosage in Treatment and Radiography, New York, The Macmillan Company, 1922.

6. Darier-Pollitzer: Textbook of Dermatology, Philadelphia, Lea & Febiger, 1920.

supported by the investigation of Siemens,[7] that the type of skin on which acne develops is an inherited one, and that constitutional disturbances, excluding the normal pubescent activity of the gonads, have little influence on acne.

PERSONAL RESULTS

Before tabulating the results, I wish to say that in no instance in this series has any permanent ill effect from the roentgen ray been seen. A slight erythema occurred during the course of treatment in twelve cases. When this happened further exposures were not given until the erythema had completely disappeared. In a number of cases a rather disfiguring tanning appeared and in two cases persisted for nearly a year before finally disappearing. This pigmentation was regarded as an indication of an increased tolerance to radiation. A few patients complained of increase in the languo hairs in the irradiated areas, but I was never able to satisfy myself that this had really occurred. All these manifestations have been extensively discussed in the literature; they are hardly susceptible to accurate estimation, and for these reasons they will not be considered further.

The average number of roentgen-ray treatments in the first course was twelve with an average total dosage of 2¾ skin units. In the second course, the average number of treatments were five, with an average total dosage of 1 skin unit.

GENERAL RESULTS

Of the 191 patients, 101 (53 per cent) were cured by one course of treatment; twenty-three (12 per cent) were greatly improved, and sixty-seven (35 per cent) had relapses. Failure to completely eradicate the disease with one course of treatment (ten or more) occurred in twenty-four instances. Twenty of these patients later reported that the disease disappeared after the treatment was discontinued.

In this study, a patient has been called "cured" when lesions did not appear after the cessation of treatment or when not more than one or two lesions were present at one time. "Greatly improved" designates those cases in which a few lesions occasionally appeared, but not in sufficient numbers to be unsightly. "Relapses" indicate a definite return of the condition, which though not as severe as the original condition in most cases, was still unsatisfactory from a cosmetic standpoint. Indeed, as the aim of treatment in this disease is to remove a cosmetically offensive condition, the designation cure, greatly improved, and unimproved or relapsed should be determined for the individual case by the cosmetic success achieved; of course, with the proviso that scars are a natural consequence of the condition, and may be disregarded.

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7. Siemens, H. W.: München. med. Wchnschr. **73**:1514 (Sept.) 1926.

RELAPSES

Table 1 is a composite tabulation of the relapses arranged according to age and also includes the final results obtained when a second course of roentgen-ray treatments was given. The second course represents the last effort of roentgen-ray treatment, since more treatment than this would appear to be beyond the bounds of prudence. At least I have not attempted more. It will be seen that twenty-three patients with relapses were permanently cured or greatly improved by this means (7 per cent of the total cases) and that in fifteen satisfactory effects were not obtained from this additional treatment. In twenty-nine cases of relapse, for various reasons, only one course of treatment was given. From these figures the ultimate result of this standard treatment can be computed as follows: There were thirty-eight cases of relapse in which a second course of treatment was given, and fifteen of these, or 40 per cent, were ultimate failures. Therefore, if the thirty patients who had relapses and who did not receive a second

TABLE 1.—*Results Arranged According to Age* *

Ages	Number of Patients	Cured and Greatly Improved	Relapses	Relapses, %	No Second Course	Cured, Two Courses	Failed, Two Courses	Final Falures, %
0 to 18	62	33	29	47	12	8	9	22
19 to 25	98	64	34	35	16	12	6	12
Over 25	28	26	2	7	0	2	0	0
Totals	188 (3)	123 (1)	65 (2)	35	28 (1)	22 (1)	15	14

* In three cases the age was unknown. These cases are placed in parentheses in the totals column. The calculation of the percentage of final failures is explained in the text.

course of treatment had actually received it, probably 40 per cent, or twelve cases (in round numbers), would have been failures. Adding those twelve cases to the fifteen actual failures, gives the total number of failures of twenty-seven, or 14 per cent of the total number of patients treated. Considering the relatively small number of cases comprised in the series this figure of 14 per cent might change in a larger series, but hardly, I believe, to any appreciable extent. It probably represents a fair figure of the ultimate failures that will be obtained by the method of treatment employed.

EFFECTS OF VARIOUS FACTORS ON TREATMENT

Influence of Age on the Efficiency of Treatment.—Referring again to table 1, it will be seen what a great influence age has on the prognosis of relapse. Rather than divide the cases into juvenile and adult, I have divided them into age periods: (1) that up to 18 years; (2) from 19 to 25 years, and (3) over 25 years. These were the ages at the beginning of treatment. The division into the three periods mentioned classes the cases into those associated with the pubescent period, those

in the acme and declining period of the disease, and those which have lasted well into adult life.

Just what influence the natural disappearance of the disease in early adult life had on the results cannot be definitely determined. That there was an influence from this source cannot be gainsaid, but this cannot change the estimate for the patient who asks concerning the probabilities of cure. The influence of age on the effectiveness of treatment or on the probability of relapse is a factor of importance regardless of the natural course of the disease—at least, the figures given indicate as much. It is worth special mention that every patient over 25 years of age was cured. This is a positive indication of the effectiveness of the treatment, since it is inconceivable that an appreciable number of these patients experienced a spontaneous disappearance of the disease coinciding exactly with the period of treatment.

Effects of Internal Disorders on the Efficiency of Treatment.—The influence of such common disturbances as constipation, focal infec-

TABLE 2.—*Influence of General Disturbances*

Diagnosis	Number of Patients	Cured and Greatly Improved	Relapsed	Relapses, Percentage
Constipation	37	20	17	46
Digestive disturbance, etc.	19	10	9	47
Focal infection	6	1	5	83
Pulmonary tuberculosis	3	2	1	33
Total	65	33	32	49

tions, digestive disturbance and other organic disturbances on the end-result of treatment is shown in table 2. In tabulating cases showing these disturbances, it was rather striking that only sixty-three patients in the whole series complained of any systemic disorder; thus, approximately two thirds of the patients were normal as to function and general well-being.

Of the thirty-seven patients who complained of constipation, twenty were cured by one course of treatment and seventeen suffered a relapse. No further analysis was made of the relapses, because the study was vitiated by the fact that constipation was treated in a routine manner. The second group comprised patients complaining of such symptomatic disturbances as headache, digestive derangement, lassitude and symptoms associated with chlorosis. Ten of the nineteen patients in this group were cured by one course of treatment, and nine had a relapse.

On the other hand, in six cases of obvious focal infections, such as chronic sinusitis, gallbladder disease and pelvic infection, five of the six patients had a relapse. These few cases do not allow any generalizations, but the result indicates that focal infections should be studied

particularly in any subsequent compilations. Chronic tonsillitis was not given any special consideration in the tabulation of focal infections, because the case records showed that many patients had had their tonsils removed in childhood, or even as a therapeutic measure for acne itself, without any apparent influence on the incidence or the course of the disease. There were three cases of arrested pulmonary tuberculosis, in two of which cure was obtained, and in the other a relapse occurred.

Relapse occurred in thirty-nine, or 49 per cent, of the sixty-five cases of systemic disturbances. This is a greater percentage of relapses than occurred in the series considered as a whole; therefore this indicated a moderately, but not decidedly, greater probability that in cases of acne associated with such systemic disturbances there will be a relapse. Perhaps even this statement may be objected to, since these conditions did receive attention (with the exception of the focal infections), and therefore the relapses are not correctly chargeable to them.

TABLE 3.—*Influence of Menstruation*

	Number of Patients	Cured	Relapsed	Relapses, Percentage
Exacerbation at period	36*	22	14	39
Menstrual symptoms	27	16	11	37
No association with menses	89	61	28	31
Total	139	99	53	38

* Thirteen of these patients had menstrual symptoms. Information about menstruation is lacking in four cases.

Influence of Menstruation and Menstrual Disturbances on the Result of Treatment.—There is a small group of women with acne in whom there is always an exacerbation of the disease at the menstrual epoch. This group may be divided into those in whom menstruation is normal and those in whom various menstrual symptoms, dysmenorrhea, menorrhagia and similar disturbances, are present. In the latter, there may or may not be an exacerbation of acne at the menstrual period. In table 3, the patients with menstrual disturbances are classified with regard to the relation of the disease to this function.

Of the 143 females in the series, only twenty-seven complained of abnormal menstrual symptoms (in thirteen of these exacerbation of the disease at the menstrual period also occurred), while thirty-six noted periodic aggravation of the disease associated with normal menstruation. In neither group was there a definite influence on the result of treatment.

Sex of Patients.—At first glance, a rather surprising thing occurred in tabulating the influence of sex. It appeared that in approximately 60 per cent of the women a permanent cure or great improvement was obtained by the first course, while in only 35 per cent of the males was a similar result achieved. Checking of the patients by sex and age

groups, however, explained the apparent influence of sex and showed that sex did not affect the result of treatment. Forty-three (30 per cent) of the 141 females whose age was known fell in the group of ages from 0 to 18, while twenty (42 per cent) of the males were in this group. Seventy-two (51 per cent) of the women were included in the age group between 19 and 25, and twenty-four (51 per cent) of the men. There were twenty-six (18 per cent) women and three (7 per cent) men in the group over 25 years of age. The reason, therefore, that the males showed a greater percentage of recurrence than the females was that a proportionately larger number of those taking treatments belonged to the earliest age group (in which relapse is most frequent) and a proportionately smaller number in the age group (over 25) in which relapse is least common. In the age group between 19 and 25, which included an equal number of the two sexes, the results obtained were practically equal; i. e., about 60 per cent of cures were obtained after the first course of treatment.

Dietary Factor.—One hundred and twenty-three patients answered the question whether or not they had followed the diet outlined. Fifty-seven had followed the diet; twenty-eight of them were cured in one course, while twenty-nine (51 per cent) had a relapse. On the other hand, of sixty-six who had not followed the prescribed diet, twenty-eight (42 per cent) were cured, while thirty-eight (57 per cent) had a relapse.

There was, therefore, a somewhat greater tendency toward relapse in the group of those who failed to carry out dietary instructions, but manifestly the difference between the two groups is not of definite significance. Collectively, the influence of diet on the result of treatment appears to be negligible, but when the patients' statements were studied, it was found that breaking the dietary regimen in some cases seemed to be the decisive factor in precipitating a relapse. It is unnecessary to describe illustrative instances in detail to prove this; several patients said that they noted a recurrence of acne only after indulging excessively in sweets and were free from the disease when they followed the diet prescribed.

Marriage.—Twenty-four of the patients were married and of this number fifteen were cured in one course, and nine had a relapse. Four of the latter were permanetly cured by a subsequent short course of treatment. The average age of the persons in the married group was 28 years, and it will be seen that marriage did not have any particular influence. If age is considered, married persons did not show greater improvement than unmarried ones in the same age groups.

Type of Acne.—One hundred and thirty-four patients had the papulopustular type of the disease, eight the superficial inflammatory

papulopustular variety and forty-nine the indurative type. The first two types were grouped together in tabulating the results, since treatment converted the inflammatory type into the common papulopustular variety before roentgen-ray treatment was begun. Ninety-three of the 142 patients with the papulopustular type were cured or greatly improved by one course of treatment, and forty-nine (35 per cent) suffered a relapse; of the forty-nine with indurative cases, thirty-one were cured and eighteen (37 per cent) had a relapse. Therefore, both types responded equally to the treatment (table 4).

RECURRENCE

Influence of Number of Treatments on Occurrence of Relapse.—In texts discussing the roentgen-ray treatment for acne, the statement is often made that even if the disease disappears after a small number

TABLE 4.—*Type of Acne*

	Number of Patients	Cured	Relapsed	Relapses, Percentage	No Second Course	Cured, Two Courses	Failed, Two Courses	Ultimate Failure,* Percentage
Papulopustular....	142	93	49	35	17	19	13	14
Indurative.....	49	31	18	37	12	4	2	14

* Calculated as in table 1.

TABLE 5.—*Effect of Number of Treatments on Relapses*

Treatments	Cured	Relapsed	Relapses, Percentage
0 to 10.....	27	16	36
11 to 13.....	36	28	44
Over 14.....	45	39	47

of treatments, it is wise to give at least twelve treatments for the purpose of preventing relapse. The additional treatments are regarded, therefore, as of prophylactic value. It seemed well worth studying this point. For that purpose, the patients were grouped into three classes, namely: (1) those who had received ten treatments; (2) those who had had from eleven to thirteen treatments, and (3) all patients who had been given fourteen or more treatments in the first course (table 5).

As a matter of fact, practically all patients in the series received one or more treatments after the disease was eradicated, and therefore the results obtained may be interpreted as indicating the value of "prophylactic" doses.

Of the forty-three patients in the first group, twenty-seven were cured and sixteen (36 per cent) had a relapse after one course; in the second group of sixty-four cases, thirty-six were cured and twenty-eight

(44 per cent) had a relapse, and in the third group, comprising eighty-four cases, forty-five were cured and thirty-nine (47 per cent) had a relapse. The difference in the percentages is not particularly significant, but they at least indicate that additional treatment for prophylactic purposes is unnecessary. It seems justifiable to conclude from these figures that the quicker the patient responds to treatment, the better the prognosis as to permanent relief. One may feel justified in stopping treatment as soon as the disease has disappeared, at least until larger figures are available.

Time of Recurrence.—There were seventy patients who gave definite answers as to the time of recurrence; of these, forty-six reported a relapse within six months, eighteen between six months and one year, five in the second year and one in the third year after treatment ceased.

Therefore, after the first year, the chance of recurrence is about 10 per cent, and studies of the permanent result of roentgen-ray treatment should be acceptable when based on a three year period of observation following treatment.

Miscellaneous.—The results of treatment in regard to the duration of the disease are not tabulated, because this factor agreed almost completely with that of the age of the patient. Likewise, the location of the disease studied by itself brought out nothing of moment.

Only twenty-nine patients were married within six months after the first course of treatment. Of these patients, twenty-two were cured and seven had a relapse. The figures are too small to be of any special importance, and besides, the course of the disease in this group parallels its course in unmarried persons in the same age class.

COMMENT

One of the striking features of this study is the number of relapses, which was larger than any previously recorded or estimated. Probably no special circumstances were responsible for this, and it remains for future studies to determine whether the figure is an average or an extraordinary one. But even though relapses occur in approximately one third of the cases, the roentgen ray is undoubtedly the most effective remedy for acne, since the final figures of 85 per cent of successes in this series can hardly be approached by any program of treatment which does not include radiation.

The decided influence of age on the probability of relapse is worthy of comment. Apparently, this has not been sufficiently appreciated or stressed. The younger the patient, the greater is the probability of relapse. The natural course of the disease appears to show that it is based on a secure foundation.

The observation that overtreatment for prophylaxis against relapse is valueless takes on an added significance when considered in the light of the influence of age; for from these two observations the logical deduction develops that only enough roentgen-ray treatment should be given to produce disappearance of the disease. In other words, as soon as new lesions have ceased to develop, roentgen-ray treatment should be discontinued. The patient should then be kept under observation and any adjunct measures that seem advisable should be continued. If a relapse occurs, radiation should be resumed until the disease has again been brought under control; of course, the limit of safety must not be overstepped. By this program of treatment, the patients that are cured will be cured by the minimum treatment necessary—a program which sacrifices nothing in efficiency and gains in safety for the patient.

SUMMARY

1. In this series of 246 patients treated by the roentgen ray and adjunct measures according to the method advocated by MacKee, no permanent untoward effect from the radiation was observed.

2. Of the 191 patients in whom the end-result of treatment has been determined, relapse occurred in 35 per cent after the first course of treatment. After a second short course of treatment, final success was obtained in approximately 85 per cent of the cases.

3. In the factors affecting recurrence, the age of the patient was the most important. Recurrence occurred in 44 per cent of patients 18 years of age or under and in only 7 per cent of those over 25.

4. Systemic disorders, such as constipation and digestive and other organic disturbances seemed to increase moderately the number of recurrences. Focal infection appeared to play a decisive rôle in the failure to cure in some cases.

5. The giving of a few additional roentgen-ray treatments after the disease was eradicated with a view of preventing recurrence proved valueless in this series. It appeared that the fewer the treatments required to cause disappearance of the disease, the less was the probability that a relapse would occur.

6. A restricted carbohydrate diet appeared not to have any influence on the efficiency of treatment when the cases were taken as a group, but dietary transgressions in some patients seemed to precipitate recurrence.

7. The following factors did not seem to have any influence on the effect of treatment: (1) menstrual disturbances or exacerbations of the disease at normal menstrual periods, (2) the variety of the disease, (3) the marital status of the patient, (4) the sex of the patient and (5) the location and duration of the disease.

8. The majority of patients had recurrences during the first six months after the cessation of treatment, and about 90 per cent of the recurrences occurred within the first year following treatment.

1017 Medical Arts Building.

ABSTRACT OF DISCUSSION

DR. HOWARD FOX, New York: I was much interested in this presentation of Dr. Michael because of my somewhat similar study. I am sorry that I have not collected my cases recently and found out the end-results, including the proportion of relapses. By a curious coincidence the number of cases in my report was exactly the same as in Dr. Michael's. If I remember correctly, the condition was entirely cleared up in three of my patients at the end of treatment, an average of thirteen treatments having been given. The acne vulgaris in forty-seven cases was almost cleared up, only a few lesions remaining, although in general the result was good. In twenty-seven cases, the result could be classed only as improvement. Many of these patients did not continue their treatment regularly. There were complete failures in two cases and relapses in four. In two patients there was a great deal of pigmentation, which finally disappeared. I was interested in Dr. Michael's statement about diet not having any particular effect in acne. I think we all feel we cannot cure patients with this disease by dietetic measures alone.

DR. WALTER J. HIGHMAN, New York: Many of the figures Dr. Michael presented are consistent with some of the impressions we received in the treatment of acne, and, when his observations and statistics come to the support of our impressions, it is satisfying. The greatest number of my failures in the treatment occurred at the same periods he mentioned. I have wanted an analysis of this. In beginning acne, when the patient is from 12 to 13 years of age, before complete development of adolescence, acne is very resistant to treatment, however mild it may be in appearance. The ordinary eruption of comedones associated with pustulation of the skin will not respond well and, if an attempt is made to treat this type with roentgen ray alone, the result will be disappointing. If this observation is correct, I should say it would be a poor policy to treat a patient with the roentgen ray when the acne was in the developing stage for fear of a failure of the optimum means of treating him when he has a florid acne later, and when he would respond to treatment. Therapy must be conserved for the disfiguring staff that might cause psychic depression. Therefore, I do not treat a patient with acne under the age of 16 by means of the roentgen ray if I can avoid it. I do not temporize because I think that it will disappear spontaneously, but because it seems to me that the period in which to obtain optimum success by this means of treatment is when the patient is between 16 and 20 years of age.

I am glad that Dr. Michael discussed diet and related theories in connection with the etiology of acne, particularly the question of menstruation. One always finds some extraordinary factor just after, before or during the menstrual period. But to reason from this that there is a causal relation between the menses and whatever is ascribed to the phenomenon has always seemed gratuitous to me. I should say that if acne always occurred in women at the same time as the menstrual period, we might consider it a factor of importance; it might even explain the inadequacy of roentgenotherapy in certain instances, but such constancy is not found. So it seems that diet, menstruation and the ordinary episodes of life do not have any bearing on the etiology of acne.

Dr. C. Guy Lane, Boston, Mass: I was particularly interested in Dr. Michael's paper because this winter I started a somewhat similar study of about 400 cases. While this is not completed, it is my impression from studying these records that the nearer the patient is to the upper edge of the age limit for acne the quicker the lesions disappear and the fewer are the relapses. Of course, there are exceptions to that rule, and the largest group includes persons with an excessive erythema at the start. Among the patients who are apt to show erythema as a result of treatment are those who have had several treatments with sulphur just previous to the roentgenotherapy, and in those cases one has to keep the dosage below the usual amount. The dosage is more of an individual matter than is generally thought.

I think Dr. Michael is right in emphasizing the discontinuance of treatment when the lesions disappear, or soon afterward; in other words, the proper method is to play safe and not run the risk of unfavorable after-effects by continuing the treatment too long. In relation to this I would like to know whether Dr. Michael has any opinion in regard to how large a total dosage will be safe for such patients.

Dr. Ernest L. McEwen, Chicago: I should like to know whether Dr. Michael has any records relative to oiliness of the skin in the cases of herpes.

Dr. Charles C. Dennie, Kansas City, Mo.: I was glad to hear Dr. Michael say that he did not think diet had much influence on acne. In the work that has been done on the metabolic rate, the urea nitrogen and blood sugar lie within normal limits in most cases.

I would like to suggest a possible etiologic factor in acne vulgaris. There may be something in it. I think that iodine has something to do with the production of acne vulgaris. It is known that small amounts of iodine will produce acne vulgaris in certain persons. I have thought that the presence of iodine in the food may effect the occurrence of acne. There are several food products which contain iodine, particularly the iodized table salts, which I always take away from patients. There is also iodine in sea foods, fats and chocolate. It may be that these foods which contain iodine may not only have a bad influence on the acne itself, but they may stimulate the thyroid gland to produce more iodine.

Dr. William H. Guy, Pittsburgh, Pa.: In adding my endorsement of Dr. Michael's paper and that type of communication, I would emphasize the importance of general treatment. These patients are apt to be lazy in their habits, and a large proportion of cases in which a relapse of acne occurred I find among those who do not pay any attention to instructions or measures directed toward improving their general health.

Dr. Harry G. Irvine, Minneapolis, Minn.: I have been using the roentgen ray in the treatment of acne for fifteen years. There are two things which I always try to do: 1. I use the roentgen ray only in the cases in which I think a reasonably good result cannot be obtained by any other means. 2. I use a smaller amount of roentgen ray than that suggested by Dr. Michael.

Like Dr. Highman, I am gratified to have some of my ideas carried out as suggested in the paper of Dr. Michael. My routine plan is to give no more than from six to eight treatments, as I find that enough in most instances, for, if the condition has not cleared up by then, it will clear up in the large percentage of cases following this course without additional treatment. In other words, I think it advisable to give six or eight treatments and then wait a month to two months instead of continuing until results appear. I think the

point should be emphasized that by doing everything possible at the same time to benefit the acne, one will find that fewer treatments of the roentgen ray are needed. My own impression is that a greater amount of scarring does not follow the use of roentgenotherapy.

Dr. John H. Stokes, Philadelphia: I should like to question the statement that ultraviolet light does not have any ill effects. Self-medication with this agency is becoming so popular that I doubt the wisdom of making a statement that it is entirely harmless. All of us have no doubt seen the extension of erythematous lupus resulting from treatment with ultraviolet light and a similar untoward result in occasional cases of psoriasis. The weathering of the skin by prolonged and frequent ultraviolet erythemas is not a negligible measure. The treatment for acne vulgaris should not be a matter of one or two methods, but of a rational application of several of them simultaneously. It is as essential to drain pustules and cysts skillfully as it is to apply the roentgen ray. A systematic attack must be made on the comedo, the primary lesion of acne. The first three or four applications of even one-eighth Holzknecht skin dose of roentgen ray in a proportion of cases give rise to a Herxheimer-like effect which makes it necessary to evacuate the maturing and early pustules in order to prevent additional scarring. The patient should, moreover, be instructed to come to the office whenever a pustule assumes threatening proportions in order to have it evacuated with the cataract knife before destruction of tissue and scarring occurs. The patient should not attempt to do this himself under any circumstances, for I am convinced that the auto-inoculation factor in acne is of real but unappreciated importance. With reference to the low carbohydrate diet, one should learn from physicians treating patients with diabetes and realize that only by the strictest adherance to a low carbohydrate regimen over a considerable period can a patient redevelop a tolerance for these foods. The average half-hearted following of a diet schedule by patients with acne is useless. The exact history of the patient with reference to dietary habits can be obtained only by having him recite his daily menu meal by meal, with attention to such items as the number of slices of bread, the number of spoonfuls of sugar in the coffee, eating between meals and at bedtime. Laxity in diet and reduction of general resistance by overwork, loss of sleep and the social whirl are prolific causes of relapse in acne vulgaris.

I feel that Dr. Irvine's statement is well made with reference to prolonged effect from a short series of moderate doses of roentgen ray. As I take this into account and insist more and more on the medical and local management of acne, I find that I use shorter and shorter series of roentgen-ray exposures.

Dr. George M. MacKee, New York: Dr. Michael's paper is valuable because of the statistics given. For the future benefit of cutaneous roentgenotherapy, we shall require statistics in addition to impressions, opinions and generalities based on experience.

It is inadvisable to depend too much on the roentgen ray. Every patient with acne vulgaris should be thoroughly examined from the standpoint of general medicine. My statistics of acne vulgaris in private practice, with end-results that are proved, consist of 316 cases over a period of eighteen years. No case is included in these statistics in which the patient was not observed for more than three years. Irritating topical applications are never used in conjunction with the roentgen ray.

The total number of patients with acne treated with the roentgen ray was 244. Of these, 147, or 60 per cent, were cured within four months; 84, or 35 per cent, required more than four months' treatment, making a total of 95

per cent. Thirteen, or 5 per cent, were failures; 37, or 10 per cent, had one recurrence, and 2, or 0.8 per cent, had two or more recurrences.

In the second series there were seventy-two patients with acne who were treated without the use of the roentgen ray. Sixteen of these, or 22 per cent, were cured within six months; 29, or 40 per cent, were cured in from one to two years, making a total of 62 per cent. Twenty-seven, or 38 per cent, were failures; 8, or 11 per cent, had one recurrence, and 1, or 1.5 per cent, had two or more recurrences.

The roentgen-ray treatment in all cases was fractional and unfiltered (one-fourth skin unit or one-fourth erythema dose once a week). One exposure was made to each side of the face at each sitting. Most of the patients requiring over four months' treatment were those who required two or three additional treatments and those who had occasional lesions and required topical treatment to complete the cure. Those with recurrences are also included in this group. Meticulous attention to hygiene and general medicine was given in each instance.

Dr. Jeffrey C. Michael, Houston, Tex.: As to Dr. Lane's question about the limit of safety of roentgen-ray dosage, I can say that the treatment given in this series did not produce permanent ill effects. The general limit of safety of roentgen-ray therapy is fairly well known. Personally, I like to stay well within the safety zone and would rather acknowledge a therapeutic failure than overstep the bounds of prudent dosage.

It did not seem to me that persons with oily skin showed more tendency to relapse than those without such a skin. Of course, a kerotic skin predisposes to acne, but the important factor in relapses seems to be the age of the patient.

The percentage of recurrences obtained by Dr. MacKee is lower than mine, possibly due to stricter attention to systemic treatment on his part. Variations in systemic treatment introduce a variable in the determination of the efficiency of the roentgen-ray treatment that can be appraised only approximately when large series of cases have been studied. Perhaps the number of recurrences in my cases was greater because I have been somewhat remiss in the internal aspects of treatment.

IMPRESSIONS OF DERMATOLOGY IN NORTH CHINA*

HARTHER L. KEIM, M.D.
PEKING, CHINA

China enjoys an extreme of climatic variation shared by no other country, as it extends from Siberia to the tropical seas. Within this vast expanse with its 400,000,000 inhabitants are to be found morbid processes of a distinctly tropical nature as well as those encountered only in frigid zones. Here, as elsewhere, nosogeography is largely influenced by climatic conditions, and in general the nature of disease processes in a particular sector is definitely related to the latitude of that portion of the country.

While sporadic case reports are available from all parts of China, little is actually known concerning morbidity and mortality figures, except in the few centers of foreign influence, since China does not possess a system for reporting vital statistics. Commendable attempts have been made toward the accumulation of such information at Hongkong, Shanghai International Settlement, Shansi province and Peking Health Demonstration Area. When one recalls the fact that about 80 per cent of China's population dwells in rural communities, and that this great group has heard practically nothing of sanitation and public health, it is possible to visualize the tremendous task confronting those interested in this problem. In the Peking area, some interesting figures are available [1] which exemplify the difficulties met in an attempt to classify disease in China. In this urban area, the population of which totals 50,000 people, 40 per cent of the inhabitants who die have not had any medical attention, 46 per cent have been treated by native physicians, who are usually self-trained, and the remaining 14 per cent have been under the care of the physicians of the district for varying periods of time. In this same center, 31 per cent of the mothers deliver themselves, 62 per cent are attended by the old style midwife, and the remaining 7 per cent are delivered under the optimum obstetric conditions that may be obtained in the average Chinese home.

From these centers, information is not yet available concerning the character or prevalence of dermatoses, although in 1900 Jeffrey and Maxwell [2] briefly classified skin conditions from reports then available

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* From the Division of Dermatology of the Department of Medicine, Peking Union Medical College.

1. Grant, J. B.: Personal communication.

2. Jeffrey and Maxwell: Diseases of China, Philadelphia, P. Blakiston's Son & Company, 1911.

and also from their own experiences, and more recently Castellani [3] and others have studied and classified cutaneous diseases as they found them in South China.

For convenience of reference, China is frequently divided into three areas; South China (to latitude 28 north) is tropical and subtropical, without any real winter season; Central China (from 28 to 35) includes the whole Yangtze Valley, with its long, warm, damp summers and cold, damp winters; North China (from 35 upward) has a comparatively dry climate, warm summers and, especially in the north, rigorous winters. It is this last division with which I am concerned, especially with the city of Peking and its environs.

At the Peking Union Medical College, one has an opportunity to gain some impressions of cutaneous diseases in North China, although such observations scarcely represent a true cross-section of dermatoses even in Peking. Many still refuse to accept modern medicine and its methods, and it is generally agreed that the Chinese patient will not often seek advice for asymptomatic conditions, a large number of which are encountered in dermatologic practice. My material is drawn from an outpatient service of over 100,000 visits a year; approximately 10 per cent of the patients are seen in the dermatologic or syphilologic clinics. Here, as elsewhere, the vast majority of dispensary patients are from the lower groups of society; coolies, soldiers, hawkers and similar groups supply by far the greatest number of cases.

PARASITIC INFECTIONS

As might be anticipated, the great majority of the dermatoses seen are various types of parasitic infestations, both animal and vegetable. Scabies, with its attendant pyoderma, is the condition most frequently seen, and on occasions one half of the new cases are acarus infections. Extensive and incapacitating pyoderma, and not the severe pruritus, is usually the factor that causes the patient to seek advice. The absence of bathing facilities in the average Chinese home and the almost prohibitive cost of water makes the treatment of scabies and other banal infections decidedly unsatisfactory. Other parasites, especially the pulex and pediculi, are of course seen; but the patient rarely consults the clinic primarily because of infestations with these organisms.

ULCERATIVE SKIN DISEASES

The various types of impetigo are common and severe, and deep ecthymatous ulcerations resembling late syphilids, especially of the legs, are seen almost daily. Furunculosis, particularly of the nuchal region,

3. Castellani and Chalmers: Manual of Tropical Medicine, Baillière, London, Tindall & Cox, 1919.

due in part to the custom of wearing a stiff cloth collar in direct contact with the posterior surface of the neck, and different varieties of folliculitis constitute a large portion of the pyogenic infections seen.

Of the great numbers of noninfectious forms of dermatitis encountered, those of known external origin account for the majority of acute cases. In China perhaps more than in western countries, the patient is first his own physician, and the local application of divers remedies results in many cases of dermatitis venenata. The pharmacopeia of China is large and mainly of vegetable origin, so that leaves, flowers, shrubs, herbs, bones and the like are used in the preparation of powders, decoctions and poultices. These are indiscriminately used by patients and native physicians alike, with little regard for their known, or rather unknown, therapeutic effect.

A favorite plaster used for the treatment of patients with localized cutaneous lesions, preferably to retain secretions, consists of a piece of paper or muslin, the size and shape of a coin. On this is applied the unknown poultice, which is usually black and glutinous; it completely covers the local lesion, which is ordinarily a deep-seated pustule or furuncle. The number of such plasters is limited only by the number of lesions, and it is not uncommon to find twenty or more such local applications. Around each lesion to which the plaster has been applied one usually finds a zone of acute dermatitis corresponding to the size of the individual plaster. In addition to home remedies and those prescribed by native physicians, the local use of foreign proprietary preparations, the supposed curative properties of which are extolled in the press, causes frequent and severe dermatitis.

DERMATITIS FROM LACQUER

Where lacquer is so universally used, one would naturally expect to find large numbers of cases of dermatitis from this known toxic agent. Cases do occur, but patients seldom come to the hospital, as the source is usually recognized and the eruption known to be self-limited. During the past year, five patients having lacquer dermatitis were admitted to the hospital. All of these were foreign patients, two of whom presented the picture of a severe dermatitis with hemorrhagic bullae.

In the shops where lacquer is used, the toxic nature of the sap of *Rhus vernicifera* is well recognized; beginners invariably suffer one or more attacks of dermatitis before they apparently develop immunity It is said that the custom of establishing immunity to this form of dermatitis by chewing the leaves of the *Rhus* tree has long been successfully practiced in the province of Szechuan, where most of the sap is collected.

LICHEN AND FUNGUS INFECTIONS

A strikingly large number of cases of chronic dermatitis are seen, mostly associated with lichenification. Neurodermatitis, especially of the neck, is often seen, which suggests the possible relationship to focci of infection which are frequent and neglected. The infrequency with which lichen planus is seen is in marked contrast to the prevalence of lichen simplex. During the past five years, not one accepted case of lichen planus has been found in Chinese patients.

Fungus infections of the skin are common and are represented by essentially the same pathogenic fungi and the same clinical characteristics as in other parts of the temperate zone. Tinea imbricata is occasionally seen, but the other tropical and subtropical fungi did not come to my attention. Persistent and rebellious involvement of the hands and feet (the latter often referred to as "Hongkong foot," presumably because of its prevalence in that city) presents as difficult a therapeutic problem in China as elsewhere.

PARASITIC INFECTIONS OF THE SCALP

Both tinea tonsurans and tinea favosa of the scalp are amazingly common, as might be inferred, especially the former. Fortunate is the Chinese boy of the poorer class who does not become infected with either parasite during his youth; since, as was pointed out by Frazier,[4] the itinerant barber uses contaminated instruments. *Trichophyton megalosporon-endothrix* can be demonstrated in the majority of the cases of tinea tonsurans, while practically all of the remainder are traceable to infection with *Trichophyton megalosporon-ectothrix*. Extensive and permanent alopecia of course occurs in tinea favosa, and one is surprised to find similar permanent patchy alopecia following many cases of tinea tonsurans. Kerion occurs but is not the rule. One is impressed with the striking infrequency of either tinea or coccogenous sycosis in Chinese patients; this is explained, no doubt, by the paucity of hairs of the bearded region. That it occurs, is demonstrated by its occasional appearance in foreign patients.

TUBERCULOSIS AND SYPHILIS

Of the great group of infectious granulomas, here as elsewhere, tuberculosis and syphilis stand preeminent. Sporadic cases of leprosy are seen, but Chihli Province has surprisingly fewer lepers than her sister state, Shantung, with its lowlands and somewhat milder winters. The mycotic infections of the group of granulomas, blastomycosis sporotrichosis and actinomycosis, are seldom seen. Kala-azar with its

4. Frazier, C. N.: Tinea Capitis in a Chinese Orphanage. China M. J. **5**:40.

massive splenic tumor is found in North China, but cutaneous manifestations of this syndrome are not encountered.

Tuberculosis of the Skin.—Tuberculosis, while not as common as in Central China, claims its victims by the thousands (approximate specific tuberculosis mortality rate 400 per 100,000 [1]), and in the medical, surgical and dermatologic clinics unusually large numbers of various types of tuberculous infections are seen daily. Cutaneous tuberculosis, while seemingly not as prevalent as in Northern Europe, is encountered with greater frequency than in America (roughly 20 per 1,000). Of the types of tuberculosis with secondary involvement of the skin, that of the glands, bones and joints is the most common, cervical adenopathy showing a striking predominance. Tuberculosis verrucosa cutis is next in frequency; the lesions may be single or, as is more often the case, multiple and extensive. In all of the patients examined during the past year, lesions were present on the buttocks, usually some distance from the anal orifice; this factor in distribution may be related to the Chinese custom of dress during infancy and childhood, which leaves the buttocks uncovered during the period when the children are habitually sitting on the ground.

Various other forms of tuberculosis, including lichen scrofulosorum, erythema induratum, tuberculosis miliaris disseminatus and tuberculosis cutis orificialis, are seemingly more frequent than lupus vulgaris. Lupus erythematosus is also infrequently seen, as are the several varieties of sarcoid.

Syphilis.—Syphilis in North China, as elsewhere, affects every structure in the human organism. While it is manifestly impossible at present to establish any worthwhile figures on the incidence of syphilis, one gains the impression that syphilis is not strikingly more prevalent among the sick in China than among similar groups in western countries. The most informative and comprehensive statistics available state that 4.79 per cent of the patients admitted to hospital beds in 1925-1926 had syphilis, which compares favorably with similar determinations made in hospitals where patients with routine cases of syphilis are cared for in the outpatient department.

As with other morbid processes that are generally painless, syphilis is often neglected, and the patients seek medical advice after other measures have failed or after symptoms occur. For this reason the chancre is usually fully developed and is seldom the only manifestation of the disease at the time of the first examination. Extragenital chancres are frequent and occur on the usual locations, with the exception of those on the lip. Instead of involving the lower lip in the midline, chancres are found on either side of the midline of the upper

lip; no doubt this is a mediate type of infection, with the chop-sticks serving as the medium of contagion.

The frequency of the involvement of the central nervous system in early syphilis was recently emphasized by Chung.[5] Late involvement of the cutaneous, visceral and nervous systems has its counterpart in cases seen in western clinics, and while cardiac syphilis in its various forms is common, aneurysms are infrequently seen.

In general, the treatment for syphilis is still unsatisfactory, and it is unusually difficult to get the patient to continue treatment as he should. The cost of arsphenamine is almost prohibitive for many, although it is dispensed at cost; but even with this factor removed, many fail to return as advised. The reasons are probably the inability to appreciate the necessity of continued treatment after the disappearance of signs and symptoms and the almost universal fear of venipuncture.

OTHER GROUPS OF DERMATOSES

A comparatively small group of dermatoses seen with more or less frequency in foreign clinics has not been recorded in North China. As was mentioned before, lichen planus does not appear on the records, nor do any of the lymphoblastomas with cutaneous involvement, although Hodgkin's disease, lymphosarcoma and leukemia are occasionally seen in Chinese patients. There is no record of pemphigus occurring in a native patient.

Allowing for economic conditions, certain racial peculiarities and the almost total lack of knowledge concerning public health and personal hygiene, diseased conditions of the skin in North China, with comparatively few exceptions, are essentially the same as those encountered in other parts of the temperate zone.

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5. Chung, Mon-fah: A Study of Thirty-Four Cases of Rapidly Developing Syphilitic Paraplegia, Arch. Dermat. & Syph. **14**:111 (Aug.) 1926.

CLINICAL EXCRETION OF MERCURY

II. AFTER INTRAMUSCULAR INJECTIONS OF MERCURIC BROMIDE, AFTER SIMPLE AND AFTER CLEAN INUNCTION *

H. N. COLE, M.D.
JOHN A. GAMMEL, M.D.
J. E. RAUSCHKOLB, M.D.
NORA SCHREIBER, B.S.
AND
TORALD SOLLMANN, M.D.
CLEVELAND

As was pointed out in the first paper of this series, the quantitative excretion of mercury is an important index of the concentration of active mercury in the tissues, and should therefore furnish data for the rational administration of mercury. A number of studies on this subject have been published, but they are not conclusive, mainly because the material was not sufficiently extensive to judge and to take account of the natural variability. Some of the studies also disregard the feces, a factor which might be important; and some of the analytic methods appeared rather questionable, at least theoretically.

We found the subject difficult; but with the collaboration of the staffs and resources of the chemistry department of Adelbert College, the department of experimental medicine, the school of pharmacy, the departments of dermatology and syphilology of Lakeside and City Hospitals and the department of pharmacology, we have been able to make steady, and on the whole, satisfactory progress. The accurate determination of these small traces of mercury in the excretion, however, is necessarily a slow process. On this account it appeared advisable to publish a report of progress a year ago, in which we attempted to evaluate the significance of the data gathered up to that time. The data were felt to be too scanty, and the current year has been devoted to the completion of these series, so that we now feel justified in replacing the tentative by definite conclusions.

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* From the Departments of Dermatology and Syphilology and of Pharmacology of Western Reserve University, with the collaboration of Lakeside and City Hospitals.

* Read before the Section on Dermatology and Syphilology at the Seventy-Eighth Annual Session of the American Medical Association, Washington, D. C., May 19, 1927.

* The expenses of this investigation have been met mainly by the Lakeside Hospital and by a grant from the Therapeutic Research Committee of the Council on Pharmacy and Chemistry of the American Medical Association.

METHOD

Analytic Method.—Booth, Schreiber and Zwick described the analytic method in 1926. The details of its application to the excreta will be discussed in a separate paper. Its accuracy has been abundantly checked, so that we have full confidence in the analytic results.

Collection of Excreta.—Three plans have been followed in the collection of the excreta. 1. By the method of continuous collection, the excreta were collected day by day, the excreta of several days often being combined for analysis. 2. By the method of periodic collection, the excreta were collected three days each week followed by an intermission of four days. 3. By the method of single collection, a single three-day specimen was gathered from a patient, usually when salivation started, or at the end of three or four weeks when treatment was about to be discontinued. The periodic collection was found the most useful arrangement, since it reflects the progressive changes during administration sufficiently to permit interpolation, and thereby saved considerable analytic work, so that perhaps three times as many patients could be studied as would otherwise have been possible. A few cases in which continuous collection is used are necessary for control. This method was generally followed at the Lakeside Hospital in the first cases of each method of administration, before the larger series was started at the City Hospital. The method of single collection appears less desirable, since it does not permit individual interpolation. With all patients except those for the single collection series, the excreta were examined for the absence of mercury before the administration was started. In a number of patients the examinations were continued for some time after the administration had been stopped, in order to study the decline of the excretion.

Administration of Mercury.—The three methods included in this paper are the following: (1) Intramuscular injection of water-soluble mercuric double-salt. Mercuric sodium bromide was employed, which is clinically identical with the mercuric sodium iodide, with the advantage that it does not complicate the analytic method. Its preparation was detailed in the preceding paper. The daily dosage of 10 mg., equivalent to 5.5 mg. of mercury, was injected daily into the gluteal muscles until salivation appeared or the course was terminated. (2) Simple inunction. Four grams of unguentum hydrargyri fortius, U. S. P. (containing 50 per cent of mercury) were rubbed into the patient's skin for thirty minutes by a nurse or orderly at the Lakeside Hospital and by the patients, under strict supervision at the City Hospital. The regions of the body were used in rotation, in the usual manner. One series of patients took the inunctions daily to the end of the course; the other series had a day of rest each week; the two

groups have been combined in the tables and graphs, because the figures do not show significant differences; in fact, the median excretion happens to run somewhat higher for the six-day than for the seven-day group. (3) Clean inunctions. These were carried out in the same manner as the simple inunctions, but the excess of ointment remaining on the surface of the skin was removed by sponging with benzene.

The number of patients examined by each method are included in table 1.

PRESENTATION OF RESULTS

The data of the patients have been plotted separately and combined, and reduced to medians and extremes, from a number of aspects. These will be presented seriatim, so as to bring out the relation of the three methods of administration.

Synopsis of Individual Patients.—The course of excretion and the significant data for each patient with periodic and continuous collections

TABLE 1.—*Number of Patients Utilized in This Study of Excretion of Mercury*

	Single Three Day Observations	Periodic Three Day Observations	Continuous Observations	Total Number of Patients
Intramuscular injections	13	3	0	16
Simple inunctions	2	7	2	11
Clean inunctions	6	9	3	18
Total	21	19	5	45

are shown in chart 1. Cases in which single collections were made are not included in this chart. There is a close similarity in the direction of all the excretion curves, and the quantitative differences between the different methods of administration are much less than the differences between the individual patients, who are arranged in ascending order of excretion under each method. The rate of urinary excretion increases progressively for at least four weeks, with all the patients. The fecal mercury also tends to increase progressively, but runs a less regular course. The ratio of fecal to urinary mercury varies widely, even for the same patient at different times.

Composite Curves of Daily Excretion.—The data of all the patients under each method, including the group in which the single collections were made, were plotted as curves on a single chart (chart 2). The individual variations within each group are much greater than the differences between the medians of the groups. A more careful study of the group differences, however, reveals important characteristics.

The group in which injections were used shows the highest excretion by the urine, the lowest excretion by the feces and the intermediate position for the total excretion.

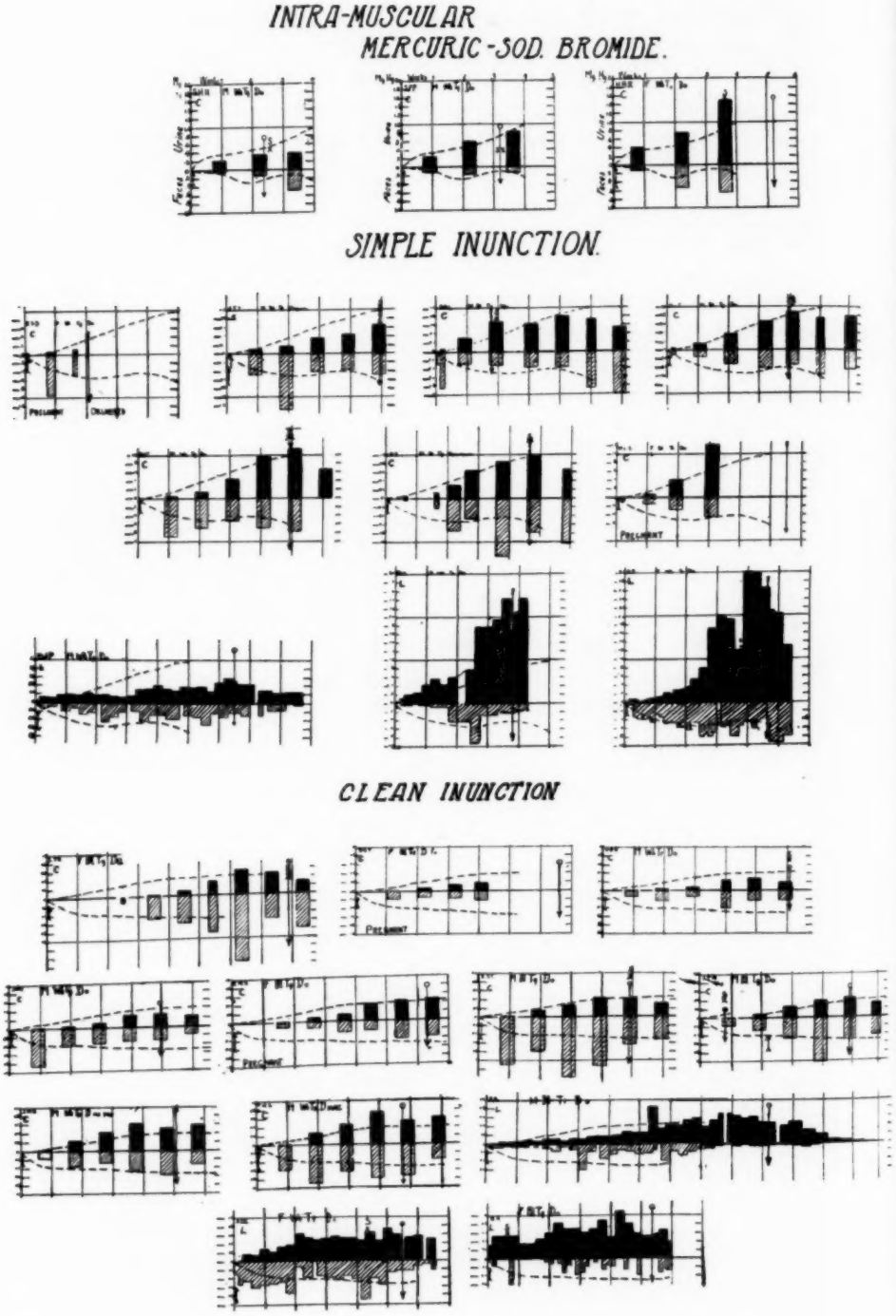
INTRA-MUSCULAR
MERCURIC-SOD. BROMIDE.
SIMPLE INUNCTION.
CLEAN INUNCTION

CHART I

Explanation of Chart I

Chart 1.—Individual charts of the patients with periodic and continuous collections. The solid blocks above the zero line represent the urinary excretion; the hatched blocks inverted below the line, the fecal excretion. The broken lines show the median excretion for all the patients on the same medication. The horizontal lines correspond to milligrams of mercury per day, each division representing 0.2 mg.; the vertical lines to the duration of the administration, in weeks. The short ascending arrow shows the beginning, the long descending arrow the end of the administration. *S* indicates the onset of salivation. The letters *x* running from left to right identify the patient, the sex (*M* and *F*); the race (*Wh* and *B*); the condition of the teeth (*T*, *e. g. f. p.* or *o*) and the cutaneous lesions (*D., o., fol., mac, pap., sqam*). *C* stands for City, and *L* for Lakeside Hospital.

The group in which simple inunctions were used shows the highest total excretion, the highest fecal excretion and the intermediate position for the urine.

The group in which clean inunctions were used shows the lowest total and urinary excretion, but the fecal excretion is nearly as high as when simple inunction was employed.

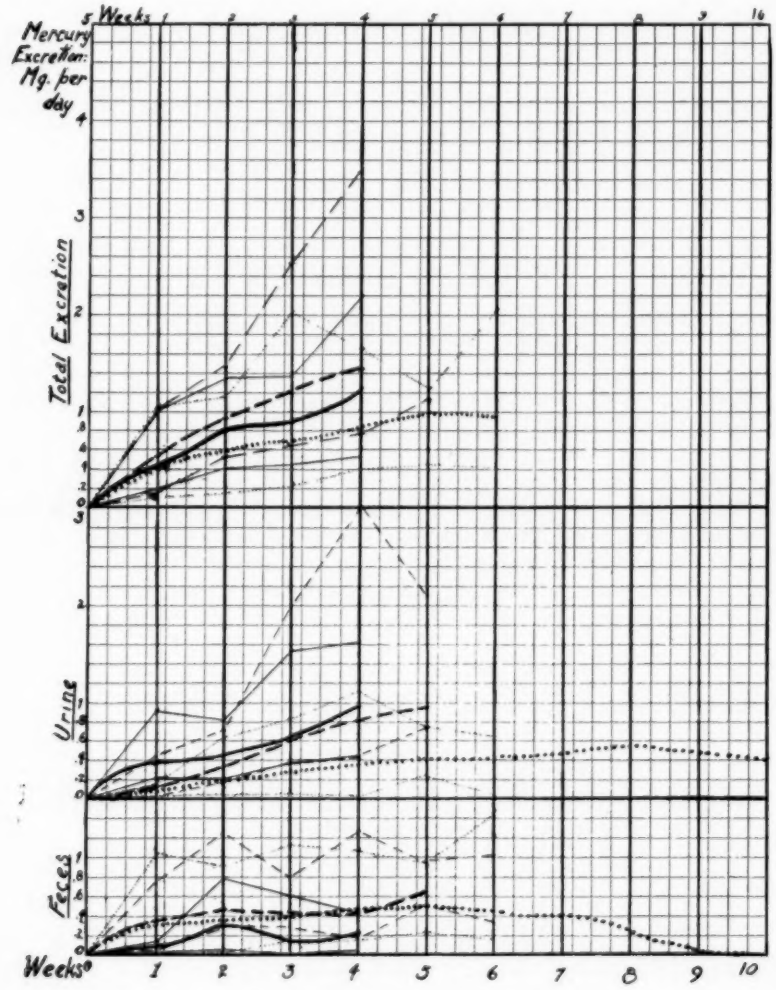

Chart 2.—Graphic illustration showing the excretion curves plotted from the data of all patients. In this and the following charts the continuous lines are the curves obtained after the injection of mercury; the broken lines, the curves resulting from simple inunction; the dotted lines, the curves resulting from clean inunction. The light lines represent the extremes of each method, the heavy lines the medians. The individual variations are shown by the areas between the light lines.

The chief significance attaches to the shift of the intramuscular injections from the highest position in the urinary excretion, to the lowest position in the fecal excretion. The reason for this shift and the numerical relations will be discussed later.

The form of the excretion curves is similar in the three methods. In all, the daily total, urinary and fecal excretion rises progressively with the duration of the administration, indicating the gradual increase of the circulating, as well as of the stored mercury. In general, the ascent of the curves tends to flatten progressively, but to a varying degree. With the clean inunctions the excretion tends to become stationary after five or six weeks, so that a balance is apparently struck between absorption and excretion, perhaps by physical saturation of the follicles of the skin. The simple inunctions and the injections were not pursued long enough to know whether such flattening also occurs. It might be expected for the simple inunctions, which would also result in mechanical saturation of the follicles of the skin; and indeed the curves tend to become flatter with time. Each injection, on the other hand, would establish an additional absorbing surface, so that it is probable that the rate of absorption could continue to increase until death. Accordingly, the excretion curve of the injections does not show the progressive flattening of the ascent. The first week also shows important differences between the methods of administration. The urinary excretion is seen to rise more abruptly with the injections, the fecal excretion with the inunctions. The initial lag in the urinary excretion of the inunctions may be attributed to the need of the chemical transformation of their mercury, before this can be absorbed. The rapid rise in their fecal mercury may be due to the accidental and almost unavoidable conveyance of some of the ointment "from hand to mouth," a subject to which we shall recur later.

After-Period.—A number of the patients were followed for variable times after the administration had been stopped. The results are plotted in chart 3 as the percentage of the secretion level at the time the administration was discontinued. This includes five patients treated with simple and seven with clean inunctions but only one who was given injections. The latter is therefore only an individual phenomenon, but the median of the inunctions should approach fairly close to the typical. It is apparent that the excretion does not stop at once; indeed it may even increase, and does so for some of the patients with each method; the extremes of the curves, however, show wide variations. Four weeks after the administration of mercury was discontinued, the total excretion was still practically at the original level for simple inunctions, and at half the level for the clean; the urinary excretion was two-thirds for the simple and one-third for the clean. In the one case of simple inunction which was followed for fifty days, the total

and the urinary excretion was still a tenth, and the fecal half of the original (total mercury, 0.34 mg. per day; urinary, 0.14 mg.; fecal, 0.20 mg.). One of Lomholt's patients also excreted 0.5 mg. of mercury forty days after the administration was stopped.

NUMERICAL DATA

The numerical data may be read from charts 1 and 2, but are sufficiently illustrated by table 2, which gives the median excretion (in

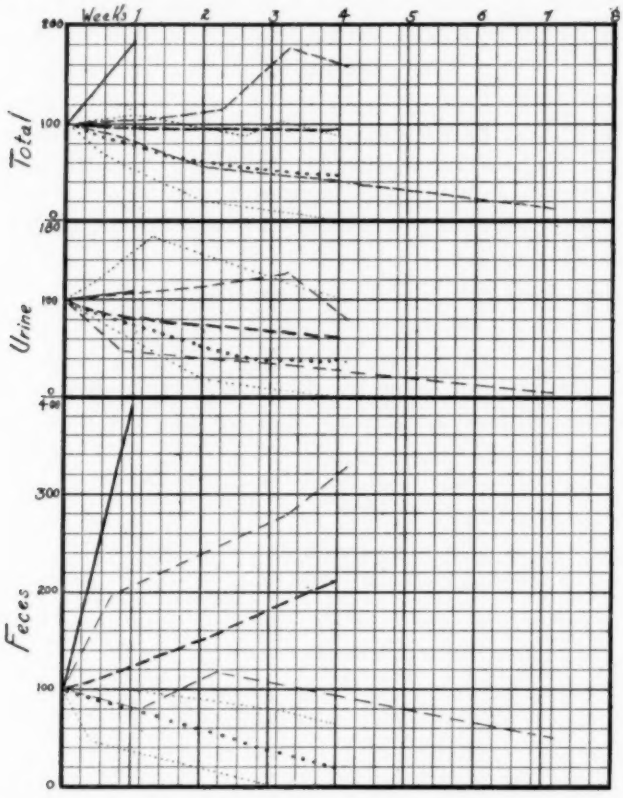

Chart 3.—Graphic illustration showing the decline of the excretion after the administration of mercury has been discontinued.

heavy type) and the range (in brackets) for each method, at the end of the first, second, fourth and sixth week. In table 3 there is an attempt to condense these data so that they can be more easily compassed, by combining the three methods. The therapeutic effects, which appear between the second and fourth week, many therefore be said generally to correspond to the daily excretion of from 0.5 to 1.5 mg. of mercury; of this, from 0.3 to 1 mg. is excreted by the urine, and from 0.2 to 0.5 mg. by the feces. The extremes of excretion in the second to the

fourth week range from 0.1 to 3.5 mg. total; from 0.03 to 2.0 mg. by the urine; from 0.01 to 1.3 mg. by the feces. The figures reported in the relatively few cases of European observers are similar to our maxima. The urinary excretion of Buergi's patient who was given injections of mercuric chloride, 10 mg. per day, was about 2 mg. at the end of the second week and 2.8 mg. at the end of the fourth; for inunctions, Buergi records about 2 mg. of urinary mercury at the end

TABLE 2.—*Daily Excretion of Mercury, Median (Heavy Type) and Extremes (Bracketted)*

		Mg. of Mercury Excreted per Day at End of			
		First Week	Second Week	Fourth Week	Sixth Week
Intramuscular injection $HgNa_2Br_4$, 10 mg. per day	Total.....	**0.46** (0.3 to 0.5)	**0.70** (0.4 to 1.1)	**1.25** (0.5 to 2.2)	
	Urine.....	**0.38** (0.2 to 0.9)	**0.45** (0.2 to 0.8)	**0.98** (0.45 to 1.55)	
	Feces.....	**0.08** (0.01 to 0.15)	**0.25** (0.1 to 0.8)	**0.3** (0.01 to 0.45)	
	Urine: Feces ratio	**4.0** (2 to 10)	**3.0** (2 to 5)	**23.0** (1 to 50)	
Simple inunction, 4 Gm. of 50% per day	Total.....	**0.56** (0.18 to 1.02)	**0.94** (0.52 to 1.45)	**1.44** (0.78 to 3.52)	
	Urine.....	**0.12** (0.02 to 0.4)	**0.33** (0.15 to 0.7)	**0.83** (0.38 to 2.0)	**0.98** (0.55 to 1.45)
	Feces.....	**0.35** (0.02 to 0.72)	**0.48** (0.30 to 1.25)	**0.45** (0.18 to 1.3)	**0.72** (0.35 to 1.05)
	Urine: Feces ratio	**0.6** (0.1 to 4.7)	**0.6** (0.1 to 2.3)	**2.3** (0.7 to 11.6)	**1.2** (0.6 to 1.8)
Clean inunction, as preceding, excess removed with benzene	Total.....	**0.41** (0.13 to 1.09)	**0.57** (0.16 to 1.18)	**0.83** (0.41 to 1.65)	**0.92** (0.40 to 2.08)
	Urine.....	**0.08** (0.01 to 0.52)	**0.24** (0.03 to 0.63)	**0.35** (0.08 to 1.10)	**0.43** (0.18 to 0.63)
	Feces.....	**0.28** (0.08 to 1.06)	**0.34** (0.08 to 0.90)	**0.51** (0.15 to 1.13)	**0.37** (0.12 to 1.55)
	Urine: Feces ratio	**0.2** (0.1 to 4.0)	**0.40** (0.1 to 5.2)	**0.8** (0.25 to 3.2)	**1.2** (0.55 to 2.2)

TABLE 3.—*Daily Excretion of Mercury, Combining the Figures of the Three Methods* *

	Mg. of Mercury Excreted per Day at End of		
	First Week	Second Week	Fourth Week
Total.....	**0.4** to **0.6** (0.1 to 1.1)	**0.5** to **1.0** (0.1 to 1.5)	**0.8** to **1.5** (0.4 to 3.5)
Urine.....	**0.1** to **0.4** (0.01 to 0.9)	**0.2** to **0.5** (0.03 to 0.8)	**0.3** to **1.0** (0.1 to 2.0)
Feces.....	**0.1** to **0.4** (0.01 to 1.1)	**0.2** to **0.5** (0.1 to 1.3)	**0.3** to **0.5** (0.01 to 1.3)

* The heavy figures are the medians; the light, the extremes.

of the fourth week; Lomholt, 1.5 mg. of total mercury at the end of the first, and 2.8 mg. at the end of the fourth week. He employed 3 Gm. of 33 per cent ointment a day, i. e., half of our dosage.

Ratio of Excretion-Level for the Three Methods.—The median data for the therapeutic period between the second and fourth week may be condensed with sufficient approximation as follows:

The total mercury for simple inunctions is about one fourth higher than with the injections.

The total mercury for clean inunctions is about one fourth lower than with the injections.

The total mercury for clean inunctions is about three-fifths that of the simple inunctions.

The urinary mercury for simple inunctions is about four fifths that of the injections.

The urinary mercury for clean inunctions is about three fifths that of the injections.

The urinary mercury for clean inunctions is about three fifths that of the simple inunctions.

The fecal mercury for simple inunctions is about three fourths more than for injections.

The fecal mercury for clean inunctions is about one half more than for injections.

The fecal mercury for clean inunctions is about one tenth less than for simple inunctions.

Dosage of the Inunctions.—The excretion following six inunctions a week is practically as high as that following seven rubs; for the clean inunctions, the median excretion happens to be even higher for

TABLE 4.—*Daily Excretion of Mercury with Six and Seven Clean Inunctions Per Week, at the End of Four Weeks*

	Mg. of Mercury per Day	
	Six Rubs per Week	Seven Rubs per Week
Total	1.0	0.65
Urine	0.42	0.27
Feces	0.56	0.45

the six day group (table 4). Further studies are under way to ascertain the effect of reducing the concentration of the ointment to 25 per cent.

Cumulative Excretion.—The action of the mercury may involve a time factor, i. e., the effect may be some product of concentration and of time of action. Data to be presented under salivation indicate that this is the case. The total quantity that has been in circulation during a given time is reflected by the total quantity that has been excreted during that time. This is represented graphically in chart 4 for the urinary and total mercury, which are especially important from this standpoint. The differences between the medians of the three methods are much smaller than the individual variations. The numerical equivalents are shown in table 5. If, for simplicity, the intramuscular injections are taken as the standard, it may be noted that the median cumulative excretion is approximately: at the end of the first week, total mercury, 2 mg., and urinary mercury, 2 mg.; at the end of the second week, total mercury, 7 mg., and urinary mercury, 5 mg.; at the end of the third week, total mercury, 21 mg., and urinary mercury, 15 mg. These medians present the rather simple relation that, as the time is doubled, the cumulative excretion is tripled.

At the end of the fourth week, the medians of the three methods compare approximately as follows:

The total mercury for simple inunctions is about one fifth higher than with the injections.

The total mercury for clean inunctions is about one fifth lower than with the injections.

The total mercury for clean inunctions is about two thirds that of the simple inunctions.

The individual variations range between one-half and twice the median.

The Retention of Mercury After Intramuscular Injection of the Drug.—In the case of the inunctions, it is possible to know how much mercury has left the body, but it is impossible to know how much more may have entered. With the intramuscular injections, the income is

TABLE 5.—*Cumulative Excretion (Medians and Extremes)*

	Total Mg. Mercury Excreted at End of			
	First Week	Second Week	Fourth Week	Sixth Week
A: Total Excretion				
Intramuscular injection	2.0 (1.1 to 2.5)	6.8 (3.6 to 9.0)	20.5 (10.6 to 34.3)	
Simple inunction	2.0 (0.5 to 3.8)	7.5 (3.0 to 12.5)	24.2 (12.6 to 48.2)	
Clean inunction	2.0 (0.7 to 5.8)	5.6 (1.9 to 11.7)	15.8 (7.0 to 33.8)	29.3 (15.4 to 47.1)
B: Urinary Excretion				
Intramuscular injection	1.96 (0.4 to 3.2)	4.8 (2.2 to 9.5)	14.4 (7.5 to 29.0)	
Simple inunction	0.9 (0.1 to 2.0)	2.0 (0.8 to 6.0)	10.7 (5.2 to 33.0)	
Clean inunction	0.2 (0.1 to 0.8)	1.1 (0.3 to 3.1)	5.4 (1.7 to 13.0)	11.0 (4.2 to 26.2)

known as well as the output; and by subtracting them, the quantity and the percentage of the amount of mercury administered that remains in the body at a given time. This "retained mercury," however, comprises three different forms: (1) the mercury in active circulation; (2) the mercury that has been absorbed, circulated and deposited in the tissues, presumably in several forms, and (3) the mercury that lies unabsorbed at the site of the injection. These different varieties have doubtless unequal significance in mercurial therapy, but for the present they must be considered together. The data are presented numerically in table 6, and graphically in chart 5. It will be seen that the excreted mercury accounts only for from 3 to 22 per cent of the amount injected, so that from 78 to 97 per cent of the mercury is retained and accumulates in the body. The percentage excreted increases with the time of administration, for instance, in the median from 5 per cent at the end of the first week, to 14 per cent at the end of the fourth week; and the percentage retained decreases reciprocally. The absolute amount retained, however, increases from 35 mg. at the end of the first week, to 130 mg. at the end of the fourth week. The variations of individual

patients in respect to the total retention are relatively insignificant; for instance the extremes retained at the end of the four weeks vary only from between 116 and 140 mg.

The Ratio of Urinary and Fecal Excretion.—This varies widely, as may be seen from the urinary fecal quotients in table 2, and in con-

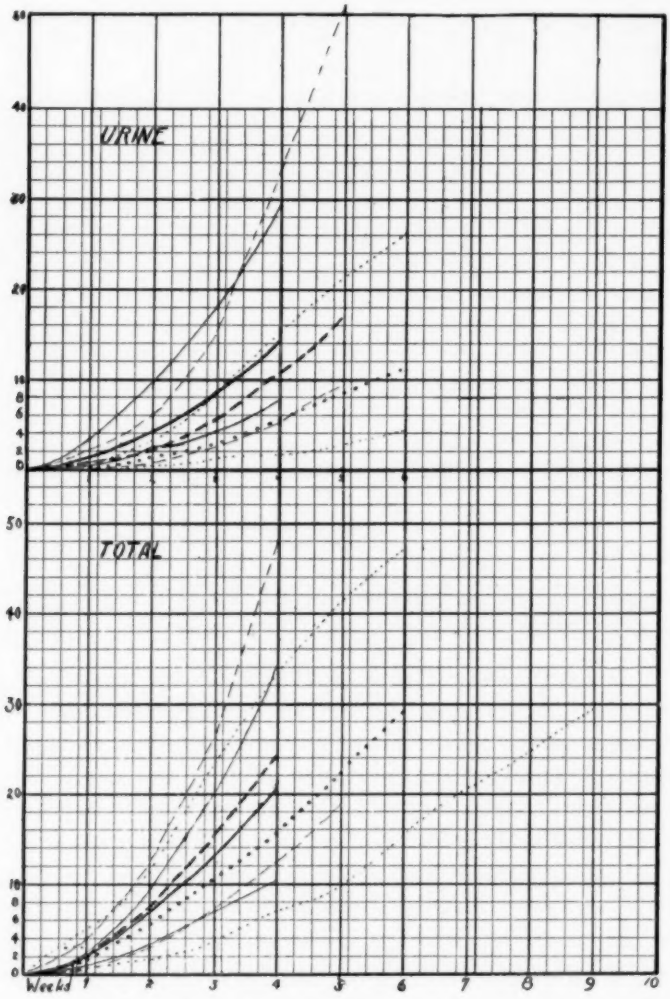

Chart 4.—Graphic illustration of the cumulative excretion of mercury.

densed form in table 7. At the one extreme the output of mercury by the urine was fifty times as great as by the feces; at the other extreme, the feces excreted one hundred times as much as the urine. Such extreme ratios were unusual and only temporary, and for a third of the determinations in each group the ratios fall within much more

restricted limits, as shown in table 7. This range, however, is still so wide that the urinary excretion may not even be an approximate index of the total excretion. It is possible that the urinary excretion may give more useful data than the total excretion in regard to special problems such as the quantity of actively circulating mercury; but this cannot be taken for granted *a priori*.

The median ratios of table 7 show that the inunctions have a much higher fecal ratio than the injections; for with the simple inunctions the feces contains nearly as much mercury as the urine, and with the clean

TABLE 6.—*Relation of Injected, Excreted and Retained Mercury*

End of Weeks	Total Administration	Maximal Excretion		Median Excretion		Minimal Excretion	
		Excreted	Retained	Excreted	Retained	Excreted	Retained
		A: Mg. of Mercury					
1	37.5	2.5	35.0	2.0	35.5	1.1	36.4
2	75.0	9.0	66.0	6.8	68.2	3.6	71.4
3	112.5	20.0	92.5	13.0	99.5	7.1	105.4
4	150.0	34.3	115.7	20.5	129.5	10.6	139.4
		B: Per Cent of Injected Mercury					
1	100	6.6	93.4	5.3	94.7	2.9	97.1
2	100	12.0	88.0	9.0	91.0	4.8	95.2
3	100	17.0	83.0	11.0	89.0	6.3	93.7
4	100	22.0	78.0	14.0	86.0	7.0	93.0

TABLE 7.—*Relation of Urinary and Fecal Mercury: Extremes and Medians for the Different Methods of Administrations*

	Urinary Mercury		Fecal Mercury One-third Within	Ratio of Fecal : Urinary Mercury		
	Range	Median		Range	Median	One-third Within
Injections.....	0.8 to 50	5.3	2.9 to 82	1/50 to 1¼	⅛	⅛ to ⅓
Simple inunctions.	0.04 to 11.6	1.13	0.55 to 1.41	1/12 to 25	⅝	5/7 to 2
Clean inunctions..	0.01 to 1.90	0.65	0.42 to 0.84	½ to 100	1½	1⅛ to 2½

inunctions, the feces contain one and a half times as much as the urine; while with the injections, the urine contains over five times as much as the feces. This difference is also conspicuous in the graphic presentation of the urinary fecal quotient in chart 6. Chart 2 illustrates that the difference is mainly due to the lower level of fecal excretion which prevails for injections.

The higher fecal ratio of the inunctions might be due to a greater deflection of cutaneously absorbed mercury toward the liver, and this in turn might be determined by the chemical and physical properties of the mercury compounds that are formed in the skin. We are inclined to advance a much simpler and rather more probable explanation, however, namely, that the patients who receive the mercury by inunction accidentally convey traces of the ointment from hand to mouth. This would

occur especially in the patients at the City Hospital who do their own rubbing; but it would occur also to some extent when the rubbing is done by others, as at the Lakeside Hospital, for the excess of mercury in the feces would correspond to less than a milligram of the ointment a day; which is probably less than the quantity that might be expected to adhere to the hands when the patient accidentally touches an area of the skin that has been rubbed. The patients at the Lakeside Hospital, however, should be expected to show a lower fecal excretion and a higher urinary fecal ratio than the general median; and this is confirmed by the figures: only one of the five patients who had received the mercury by inunction at the Lakeside Hospital excreted the median

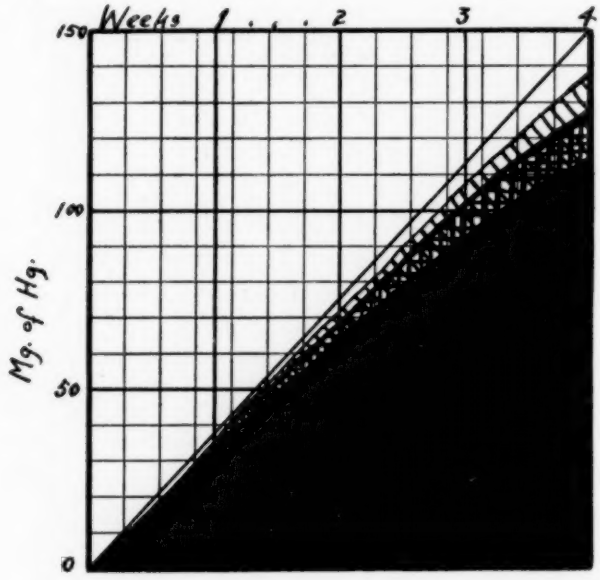

Chart 5.—Graphic illustration of the relation of the amount of mercury excreted and retained. The diagonal line from 0 to 4 represents the amount of mercury administered; the light portion below this line, the amount excreted and the black portion, the amounts retained.

quantity of fecal mercury; the other four excreted materially less (chart 1). The urinary: fecal quotient of the patient at the Lakeside Hospital who received mercury by simple inunction was 5.1 and 11.6 instead of the median 2.3; and for clean inunctions, 0.8, 1.3 and 3.2, instead of the median 0.8. If this explanation is correct, a part of the mercury that was swallowed would presumably be absorbed and part of the effects of the inunctions may be due to the oral absorption. This may also explain the greater urinary excretion of the simple over the clean inunction, for it might be expected that the excess of

ointment of the simple inunction would increase the occasions for oral conveyance. The possibility of this oral route must be considered as a source of error in the interpretation of the cutaneous absorption of mercury, which could perhaps be avoided by elaborate precautions; but this is not material for our present object, since this is concerned primarily with the administration of mercury of actual clinical practice.

Chart 6 also shows that the urinary: fecal quotient tends to rise with the duration of the administration, and chart 2 shows that this is due to the progressive increase of the urinary excretion after the fecal excretion has become practically level. This might be expected for the inunctions, since the fecal excretion would be influenced more by the unabsorbed mercury from the oral income, which would remain constant, while the urinary excretion would rise with the increasing absorption of the mercury from the fuller skin depots. Another explanation, however, would have to be sought for the intramuscular absorption.

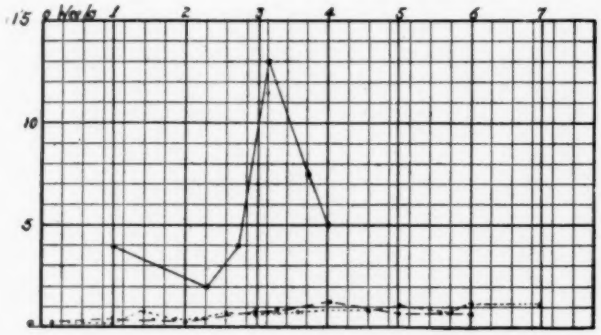

Chart 6.—Graphic illustration showing the urinary: fecal quotient.

FACTORS THAT HAVE AN INFLUENCE ON THE AMOUNT OF EXCRETION

The Relation of the Volume of Urine Excreted to the Mercury It Contains.—It is interesting from several points of view to know whether diuresis and catharsis or their converse influence the rate of the urinary excretion. The cases in which the method of continuous collection was used are best suited for this purpose, and the complete data were plotted for four such patients, two each on simple and on clean inunctions. All the significant phenomena, however, may be illustrated on the two patients plotted in chart 7. The mutual relations of the volume and oscillations of mercury may be judged after the second or third week, when the excretion of mercury had reached a nearly horizontal direction. It will be noted (chart 7, at *a*) that the volume of urine may undergo considerable oscillations without any change in the daily excretion of

urinary mercury. On the other hand, marked oscillations in the excretion of mercury are generally accompanied by changes in the volume of urine, but these may be either in the same direction (at *b*), or as often in the opposite direction (at *c, c*). It seems therefore, that the rate of secretion of urine has no constant effect on the level of excretion of urinary mercury, and is probably of little importance.

Excretion of Urine During a Course of Mercurial Inunction.—The output of urine does not undergo any material change during the course of mercurial inunction (chart 7).

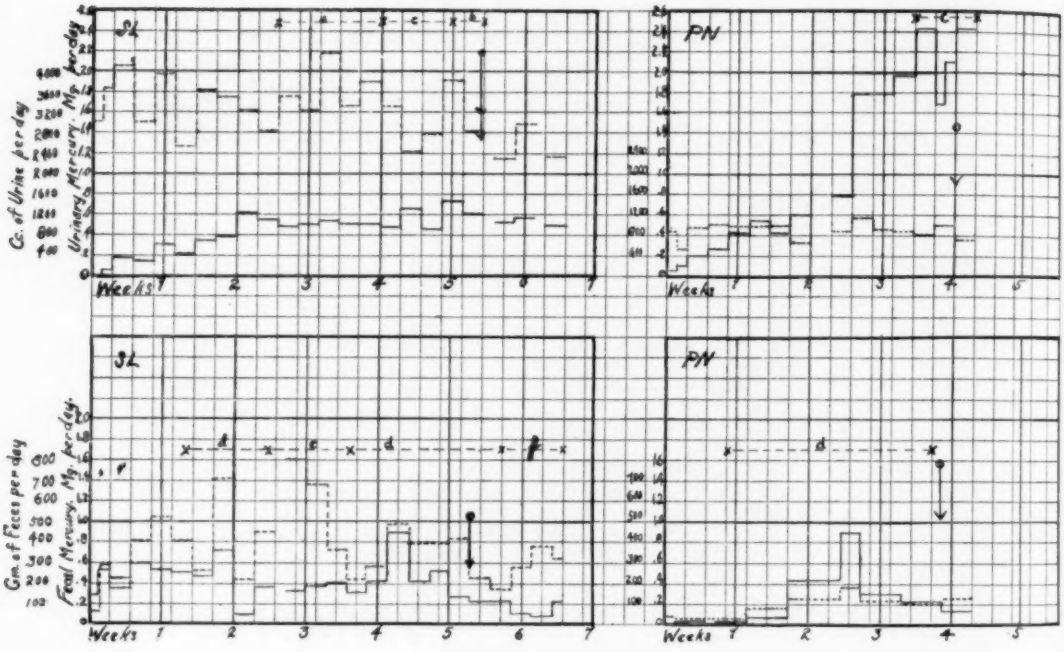

Chart 7.—Graphic illustration showing the relation of the volume of urine and weight of feces to the excretion of mercury. The dotted line represents the volume of urine; the solid line, the mercury it contains.

Relation of the Weight of the Feces to Their Content of Mercury.—There is a definite tendency for the weight of the feces and the excretion of fecal mercury to run parallel, as in chart 7, *d, d, d.*, but occasionally, considerable changes in the weight of the feces may occur without altering the amount of fecal mercury (at *e*); sometimes an increase in the weight of feces may be accompanied by a decrease in the amount of mercury contained in them.

Effect of Mercurial Inunction on the Weight of the Feces Excreted.—The amount of feces tends to increase during the first two or three

weeks of the inunctions, and then to decrease toward the normal amount even though the inunctions are continued (chart 7).

Personal Factors That Influence the Amount of Excretion of Mercury.—Individual variations in the excretion of mercury are much greater than the differences between the methods of administration, as expressed by their medians (charts 1 and 2). It would be interesting and of practical importance to know the causes of these differences. This has been attempted by grouping the patients according to sex, color and active lesions of the skin, and then counting the number of patients of each group whose excretion level was (*a*) materially above the median of those receiving mercury by that method of administration, (*o*) practically on the median and (*b*) materially below the median. For convenience, this was expressed as a single figure; so that 5.1.3 would mean five patients whose excretion level was above, one on, and three below the median excretion. The frequency distribution was

TABLE 8.—*Distribution of Excretion Level According to Sex and Race*

	White		Difference M - F	Black		Difference M - F
	Male	Female		Male	Female	
Injection: Total.....	3.0.4 = −1	1.0.1 = 0	−1	0.0.1 = −1	1.0.0 = +1	−2
Urine.....	2.1.5 = −3	2.0.1 = +1	−4	0.1.2 = −2	1.0.0 = +1	−3
Fecal.....	2.0.5 = −3	0.0.2 = −2	−1	0.0.1 = −1	0.1.0 = 0	−1
Inunction: Total.....	7.0.2 = +5	1.1.0 = +1	+4	4.0.5 = −1	1.1.5 = −4	+3
Urine.....	6.1.2 = +4	2.0.0 = +2	+2	2.4.3 = −1	3.0.4 = −1	0
Fecal.....	5.1.3 = +2	1.1.0 = +1	+1	4.3.2 = +2	0.3.4 = −4	+6

calculated by subtracting the two extreme figures in the foregoing example, 5.1.3, and this gave an excess of + 2; if the figure had been 2.3.9, the excess would have been — 7; "+" standing for excess above, and "—" below the median. The difference between the two examples (+ 2 and — 7) would be + 9 in favor of the first series. This method is a convenient index of differences in the distribution of the results above and below the median. More elaborate statistical methods would scarcely be justified in view of the relatively small number of data that result from these groupings. We are aware of these limitations, and have hesitated before submitting even tentative conclusions; however, when the results tend rather consistently in certain directions, they appear to deserve some consideration. The data for sex and race are shown in table 8.

Influence of Sex on Excretion Level of Intramuscular Injections.—The excretion is consistently lower in men (table 8). This is especially true of the mercury in the urine; hence it would appear that the concentration of circulating mercury is higher in women. This would be expected, at least in active tissue, since the average weight of women

would be lower, while the quantity of mercury administered was the same for both sexes.

Influence of Sex on the Excretion Level of Inunctions.—The simple and clean inunctions are calculated together to give larger numbers. In contrast to the results after injections of mercury, the inunctions show distinctly greater excretion for men. Two explanations occur to us: First, the men would be likely to rub vigorously, thereby securing greater absorption; second, men may have been more negligent about their hands, and so have conveyed more of the mercury to the mouth. Probably both factors played a part, but to a different degree in the white and in the colored races. In colored men, the great predominance of fecal mercury and the absence of any difference in the urinary mercury point strongly to the hands as the cause, as might be expected, since the ointment would not be readily seen on the colored skin. For white

TABLE 9.—*Differentials of Excretion Level for Race (Differentials Whites Minus Negroes)*

		Males	Females
Injections:	Total	0	−1
	Urine	−1½	0
	Feces	−2	−2
Inunctions:	Total	+6	+5
	Urine	+5	+3
	Feces	0	+4

men, on the other hand, the chief factor is probably the rubbing, for the fecal mercury shows less difference than the urinary.

Relation of the Excretion Level to Race.—In table 9, the differentials of table 8 are rearranged to show their relation to race. With the intramuscular injections, the differences are small, irregular and probably accidental, but so far as the data go, the white patients excreted somewhat less mercury than the negroes. With the inunctions, the white patients excreted considerably more mercury than the black, indicating either that the white patients rubbed more vigorously or, what is more probably the major factor, that the structure of the white skin (especially in respect to the glands) facilitates the absorption of mercury.

Diligence in Inunction.—Although the inunctions were supervised, it was impossible to make every patient rub with equal energy. This doubtless accounts for some of the differences in the excretion level. In order to estimate these factors, the patients were grouped according to their willingness to cooperate. Application of the differential method to this grouping gave the following result:

These differentials indicate a tendency for those who rub energetically to reach a higher excretion level, and those who rub negligently,

a lower level; but they also show some high levels for those who rub negligently and low levels for those who rub energetically; so that the energy with which the inunction is made may be more than offset by other factors.

Influence of Acute Dermatitis on the Absorption of Mercury.—Some of the clinical members of our group had the impression that the absorption of mercury from inunctions would be higher when these are applied over acute cutaneous syphilids. Such lesions were present in six of the patients receiving inunctions in this series. In three of these patients, the excretion level was found to run distinctly above the median, but in an equal number it ran just as distinctly below the

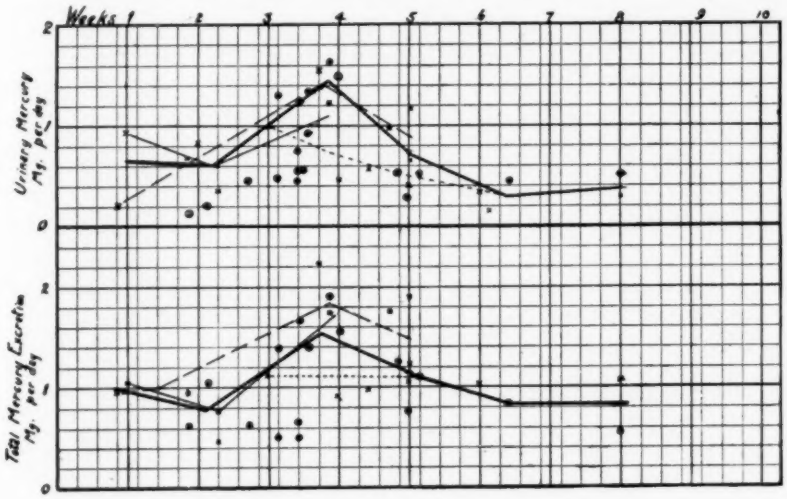

Chart 8.—Graphic illustration of the relation of salivation to the level and time of excretion. All methods of administration of mercury are represented by a heavy continuous line; injections by a light continuous line; simple inunctions by a broken line; clean inunctions by a dotted line; the earliest sign of salivation by a cross and the time when the administration was discontinued before salivation began, by a circle.

median; so that the clinical judgment has not been confirmed. It may be added that the salivation data in these cases agreed with the chemical observations.

Relation of Salivation to the Excretion Level.—The relation of salivation to the level and time of excretion was studied by plotting the time of onset of salivation against the daily urinary and total excretion, as shown in chart 8; the excretion of mercury being charted vertically, and the time horizontally. In the working chart these data were kept distinct for the three methods of administration; but in the final chart the methods are distinguished only by their median curves. Chart 8 shows that the direction of these is so similar for the urinary and total

excretion, that it may suffice to center the attention on the urine curve; and for the present, on the heavy line that represents the general median of the three methods. It will be noted that the median level of daily output of urinary mercury at which salivation occurs, which we may call the "salivation level," ascends from about 0.65 mg. at the end of the first and second week, to a peak of 1.4 mg. at the end of the sixth week, where it remains. The curve therefore presents two phases, separated by a "critical point" about the end of the fourth week. The patients who salivate before this time do so before a high level of mercury has been reached, presumably because they have a special susceptibility for mercurial salivation. After the fourth week, the especially sensitive patients have been weeded out; and from here

TABLE 10.—*Cooperation of Patients Calculated by Differential Method*

	(a)	(o)	(b)	
Cooperation excellent	2	1	1	= +1
Cooperation satisfactory	1	2	2	= −1
Cooperation fairly satisfactory	0	0	3	= −3
Cooperation unsatisfactory	1	0	2	= −1

TABLE 11.—*Correlation of Salivation and Mercury Excretion Level*

Methods of Administration	Percentage of Patients Salivated by the End of the Fourth Week	Median Urinary Mercury (Mg. per Day) at the End of the Fourth Week
Intramuscular injections	66	1.44
Simple inunctions	39	0.83
Clean inunctions	9	0.45

on, the salivation level descends with the duration of the administration, as a fairly smooth curve; in other words, after four weeks, the lower the level of excretion of mercury, the longer is the time required to produce salivation. Moreover, if one excepts the relatively few early cases of special susceptibility, the remaining cases are clustered fairly close to the median curve; so that in a considerable majority of patients the intensity and duration of the excretion of mercury are the chief factors in determining salivation. This confirms the clinical impression that mercurial stomatitis is a fair index of the intensity of mercurial medication in most patients, but that there are individual exceptions.

Comparison of the Three Methods of Administration.—The salivation level lies somewhat lower for the clean inunctions (chart 8); this may be due to the somewhat lower rate of absorption and a correspondingly longer duration of administration before the level was reached. The difference, however, is not significant. On the other hand, there is a striking relation between the percentage of patients that have

become salivated at the end of four weeks, and the urinary excretion level with each method, as shown in table 11.

Relation of Salivation Level to Other Factors.—The differential method described for the correlations of the excretion level was applied to these problems, the patients being classified with reference to the median urinary salivation level. This was tried on the factors of race and sex with the following results:

It is seen that there is no difference in salivation level between the races and only a slight and probably accidental difference between the sexes. This is as would be expected and is therefore a confirmation of the applicability of the method.

TABLE 12.—*Relation of Salivation Level to Other Factors Calculated by Differential Method*

		(a)	(o)	(b)		Difference
Male	White	4	3	4	= 0	
	Black	1	4	1	= 0	0
Female	White	3	0	2	= +1	
	Black	2	0	1	= +1	0
All whites		7	3	6	= +1	
All blacks		3	5	2	= +1	0
All males		5	7	5	= 0	
All females		5	1	3	= +2	2

TABLE 13.—*Salivation Level in Relation to the Condition of the Teeth Calculated by Differential Method*

Condition of the Teeth	Rating (a)	(o)	(b)	Differential
None	2	0	1	+1
Excellent	2	2	1	+1
Good	4	5	4	0
Fair	2	1	2	0

Relation of Salivation to the Condition of the Teeth.—This is usually supposed to be next in importance to the intensity of the mercury medication. The condition of the teeth was noted in all the patients before their medication was started, and in the end these records were compared with the median salivation level:

The salivation level is therefore somewhat higher for "excellent" and no teeth than for "good" and "fair" teeth; but the differences are so slight that they are uncertain; and it is doubtful whether salivation is influenced at all by conditions of the teeth ranging from the "fair" to "excellent," at least if the hospital customs of oral hygiene are followed. There were no "poor" teeth in the group. Further studies will doubtless add more data to this subject.

SUMMARY

The urinary, fecal and total excretion of mercury was studied in three groups of patients treated with intramuscular injections of mercuric sodium bromide (10 mg. per day), simple inunctions, and inunctions with subsequent removal of excess ointment by benzene. The variations between different patients treated by the same method were much wider than the differences between the medians of the different methods. In all, the rate of excretion increases with the duration of the administration, but at somewhat different rates. At the end of the usual three or four weeks' course, the total daily excretion averages from 1 to 1.5 mg.; the extremes, from 0.5 to 3.5 mg. With simple inunctions, it averages about a fourth greater, and with clean inunctions about a fourth less, than with the injections. The ratio of mercury in the urine to that in the feces varies widely. The urinary excretion is relatively higher after intramuscular injections; the fecal excretion after inunctions. This is probably due to the conveyance of some of the ointment from the hands of the patient to the mouth. The total amount of mercury excreted in the four weeks' course of injections averages 21 mg., of which 15 mg. is in the urine. With simple inunctions, the total excretion is about a fifth greater, and with clean inunctions, about a fifth less. After discontinuance of the administration, the excretion continues high for a considerable time.

The volume of the urine has no constant effect on the urinary excretion of mercury; the fecal excretion tends to vary with the weight of the feces.

After intramuscular injections of mercury, women excrete more of this drug than men do, presumably because of the higher relative dosage. When the method of inunctions is used, men excrete more than women; this is attributable to more vigorous rubbing; negroes excrete more than white patients (less thorough removal of ointment from hands?).

In most patients the salivation depends on the intensity and on the duration of the excretion of mercury; but patients hypersusceptible to stomatitis may develop this condition early, when the excretion level of mercury is still low.

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ABSTRACT OF DISCUSSION

DR. FRED. M. JACOB, Pittsburgh: Mercury was used on an entirely empiric basis, and that empiricism is still to be noted in the method of administration and the kind of drugs we use. Many things have been of assistance in curing some

of the ills and correcting some of the errors that were present because of the physician's insufficient knowledge. Drs. Cole's and Sollmann's work will help us to treat patients with syphilis more effectively and possibly to cure them in a shorter time. Regarding inunctions, a number of workers have shown that the inunction method and form of drug used by Dr. Cole were probably the best for the administration of mercury through the skin. Although his clean inunctions seem to be effective clinically and in the work presented here, they are slightly inferior to the other inunctions. The work of Kolmer and others does not agree with these observations but Dr. Cole also shows that the amount of mercury taken by mouth has some influence on the amount of mercury absorbed and excreted by these two methods. Excretion rises rapidly when intramuscular injections of soluble salts are used, and most physicians agree that this is the best route of administration. Kolmer and others show great destruction of muscle structure by the use of injections of soluble mercury, but this does not seem to be any objection to the clinical use of the drug. As excretion rises rapidly with injections, but continues higher with inunctions, a combination treatment starting with injections and ending with inunctions would comprise a good method for saturating patients with mercury, which is the aim in the use of this potent drug, and would give the best possible chance of clearing up the syphilis early.

The question of the excretion of mercury in the circulating blood has been brought up previously, in relation to the great bugbear of the Wassermann reaction. I think Dr. Cole has shown us the necessity for some type of treatment that will give a more rapid elimination of the store of mercury in the body and permit a fresh start at the end of the rest period. When one considers that fifty days after the administration of mercury the excretion is still one tenth, and it is known that the spirochetes develop immunity, it seems to me that it would be well if we could develop some method of eliminating the mercury before the next course of treatment. We administer the drugs in courses, with rest periods between, and if we can rid the body of this store in the interval, we can make a great advance in this treatment.

Dr. F. J. Eichenlaub, Washington: An important feature of the work of clarifying the method of action of mercury is that it keeps before one the fact that mercury is of great importance in the treatment of patients who have syphilis. There is a marked tendency on the part of the general practitioner and of some specialists to supplant mercury with bismuth. I think this is a mistake.

Dr. Harold N. Cole, Cleveland: Because of lack of time, I did not say anything about our belief that the patient probably absorbs a certain amount of mercury by mouth. That may explain in part the high amount of mercury which is found in the feces following the use of inunctions. I spoke of the case of the patient who was followed for fifty days after the inunctions were stopped.

Dr. John H. Stokes, Philadelphia: I suggest the desirability of a little propaganda for the authority of the public health service to test drugs for therapeutic effect as well as for toxicity.

INCOMPLETE FORM OF VON RECKLINGHAUSEN'S DISEASE

REPORT OF CASES *

JOSEPH JORDAN ELLER, M.D.
NEW YORK

In 1925, Wise and Eller [1] reported several cases of von Recklinghausen's disease without tumor formation, with a review of the literature, before the Section on Dermatology and Syphilology at the seventy-sixth annual session of the American Medical Association. In the discussion which followed, some of the members were not in accord with the ideas presented, and some openly doubted the existence of von Recklinghausen's disease without tumor formation.

Since that time, I had the opportunity to observe two families in which some of the members presented the incomplete form of von Recklinghausen's disease.

CASE 1.—F. F., a woman aged 33, married, childless, was first seen on April 2, 1927, suffering from a folliculitis of the pubic region. At the time of the examination, there were numerous pigmented areas on various parts of the body which varied from dark yellow to brownish; they tended to be more numerous on the trunk. These pigmented patches varied in size, some being as small as a pea and others as large as 7 cm. in diameter. A careful examination failed to reveal any tumor formation. The patient was also seen by Dr. MacKee, who agreed with the diagnosis of von Recklinghausen's disease without tumor formation.

The following family history was obtained: The paternal grandmother had had numerous pigmented areas on her body, but as far as was known, tumors had never developed, and she had died at the age of 77. The paternal grandfather had not had any skin abnormalities and had died at the age of 70. The patient's mother was 67, living and well and did not have any abnormalities of the skin, while the patient's father, aged 67, began to have small tumors at the age of 30 which had grown larger and more numerous during the past twenty years. A sister, aged 42, had numerous pigmented areas of the skin and a few small tumors. The tumors did not appear on the skin of this sister until the age of 35, although the pigmented patches had been present for many years. Another sister, aged 39, had many small nodular tumors of the skin. These began to appear when she was 10 years old. There were no other children.

CASE 2.—A. F., a woman, aged 40, presented the classic picture of von Recklinghausen's disease with pigmentation and tumors. Fifteen years ago she first noticed pigmented areas and small tumors on her body. Since that time these have become more numerous. Neither her parents' history nor that of her three

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* From the New York Post-Graduate Medical School and Hospital, Department of Dermatology and Syphilology.

1. Wise, F., and Eller, J.: Von Recklinghausen's Disease Without Tumor Formation, J. A. M. A. **86**:86 (Jan. 9) 1926.

brothers and four sisters contained anything suggestive of von Recklinghausen's disease. One brother had died at the age of 28 from Hodgkin's disease. The history was negative on her husband's side.

This patient had four children, two boys and two girls. The oldest child was a youth, aged 20, who presented a few pigmented areas on his back but he did not have tumors. The second child was a girl, aged 16, who had irregular, pigmented areas on the trunk and limbs varying in size from that of a walnut to that of a dollar. These had been present since birth. She did not have any tumors. The third child, a boy, aged 11, did not present pigmentation or tumors, but had a definite lateral dorsal curvature of the spine. The latter condition has frequently been seen in patients with von Recklinghausen's disease. The fourth child was a girl, aged 3 years and 6 months, who presented numerous pigmented areas which varied in size from that of a dime to that of a quarter and larger; these had been present since birth. She did not have tumors.

From a consideration of the foregoing case reports and other similar reported cases, there is no doubt that an abortive, incomplete or pre-tumor type of Recklinghausen's disease exists and can be recognized.

The conclusions stated by Wise and me may be reiterated:

1. The cutaneous manifestations of von Recklinghausen's disease consist, in a certain group of cases here described, of nothing more than widely scattered pigment spots irregularly distributed on the trunks, buttocks and thighs. They vary from a light yellow to a deep brown, and from pinhead-sized freckles to extensive areas, large enough to cover a buttock or a thigh, or a large area of the trunk.

2. This tumorless variety of the affection is usually encountered in one or more children of a family in which either parent has a typical neurofibromatosis cutis, as originally described by von Recklinghausen. However, a pigmentary eruption without tumors may also occur in adults.

3. To this variety of von Recklinghausen's disease the terms "incomplete" and "abortive" have been applied, suggesting the assumption that as the disease progresses, tumors *eventually will make their appearance.*

4. The terms neurofibromatosis cutis or fibroma molluscum multiplex are applicable only to those cases in which tumors form a part of the clinical picture.

100 West Fifty-Ninth Street, New York.

PELLAGRA

WITH SPECIAL REFERENCE TO THE SKIN AND MUCOUS MEMBRANE *

EARL D. CRUTCHFIELD

GALVESTON, TEXAS

Pellagra, like most diseases which occur endemically, begins to show changes in its clinical manifestation as adaptation to environment occurs or as the disease becomes milder. In order to determine these clinical manifestations, a study was made of 125 cases of pellagra, occurring in the John Sealy Hospital in Galveston, special attention being paid to the conditions of the skin and mucous membrane.

Pellagra originated in the United States in 1902,[1] but first received attention in a report from Alabama in 1906.[2]

Much has been written on the etiology, symptomatology and pathology of the condition. Speculation and theory have ranged from the probability of infection from spoiled maize to the factors of intoxication and diet and the later vitamin theories.[3] At present some unknown factors in the etiology of pellagra still remain.

Some months ago, I became enthusiastic on finding a spirochete in the blood in three of ten persons with pellagra, only to have my enthusiasm dampened on learning that similar spirochetes may occur in other cachetic conditions.

The scope of this paper includes the course and clinical manifestation of pellagra in the skin and mucous membranes with the pathologic conditions in the blood, urine and special fluids; a consideration of factors which may have a bearing on the development of the disease, such as sanitation and habits, and predisposing, and concomitant diseases. The results of treatment are included.

Sixteen cases of the 125 diagnosed as pellagra were discarded. While these cases were believed to be pellagra, they did not present the classic signs and were classified as pseudopellagra. One hundred and nine cases, therefore, were reviewed.

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* From the Department of Dermatology and Syphilology, University of Texas.

* Read at the Fiftieth Annual Meeting of the American Dermatological Association, Baltimore, May 12-14, 1927.

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2. Silver, J. F.; Garrison, P. E., and Mac Neal, W. J.: Third Report of the Robert M. Thompson Pellagra Commission of the New York Post Graduate Hospital and Medical School, South. M. J. **11**:786, 1918.

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There were 46.4 per cent of negroes in this series, slightly more than the number usually reported from the southern states.[4]

Seventy-four and six-tenths per cent of the patients were females, corresponding to the usual observations in the South.[5]

Eighty and seven-tenths per cent of these cases originated in the city, 18.25 per cent in small towns or the country. Only 17.15 per cent came from areas with rural sanitation, which did not suggest drainage as a factor in the occurrence of the disease. The marital relation was not suggestive. There were forty-two housewives and twenty-nine women employed as domestics, fifteen laborers and seventeen with professional or clerical positions. Fifty-three and forty-seven hundredths per cent were shown to have an adequate supply of food available. Twelve lived on carbohydrates without meats, while twelve presented disease conditions which prevented proper nourishment. History of contact was not recorded in any patient.

The age incidence ranged from four to eighty-one years, with the greatest number in the third and fourth decades.

Eighty-two of the 109 were seen in their first attack. The major pellagrous symptoms complained of were as follows: diarrhea in 35.31 per cent, mental and nervous symptoms, including paresthesias in 26.23 per cent, lesions of the skin in 19.17 per cent, lesions of the mucous membrane in 9.08 per cent, weakness in 7.06 per cent, and gastro-enteric symptoms in 13.11 per cent.

Forty-eight and forty-three hundredths per cent suffered from diarrhea, 23.20 per cent had obstinate constipation, 10.09 per cent had diarrhea alternating with constipation and 19.17 per cent did not have any colonic symptoms.

CONTRIBUTORY DISEASE

In a study to determine factors which might be contributory to pellagra, it was seen that most of the patients gave a history of some specific, previous disease which disturbed nutrition, suggesting the possibility that pellagra is often a secondary disease such as recently described by O'Leary [6] as secondary pellagra. Seventy-four and sixty-six hundredths per cent gave a history of melancholia, gastro-enteritis, colitis, overwork, worry or strain, syphilis, alcoholism or carcinoma which directly or indirectly interfered with nutrition. Six and five hundredths per cent had gastric obstruction, 16.14 per cent had pelvic disease, four

4. Siler, J. F.; Garrison, P. E., and Mac Neal, W. J.: Studies on Pellagra, Arch. Int. Med. **14**:293 (Sept.) 1914.

5. Harris, Seale: Food Conditions in Europe with Remarks on the Etiology of Pellagra, New Orleans M. and S. J. **72**:452 (Feb.) 1920.

6. O'Leary, Paul A.: Secondary Type of Pellagra, M. Clin. N. Amer. **10**:647 (Nov.) 1926.

had stricture of the rectum and one cancer of the colon. On analysis 85 per cent showed some definite pathologic condition which might be considered contributory.

In 54.48 per cent of the cases, giving rise to the major symptomatology, there was some concomitant major pathologic process which equaled or overshadowed the pellagrous syndrome.

Two patients illustrated the bearing absorption may play in the production of pellagra. A middle-aged negress developed a bilateral, symmetrical dermatitis while under observation in the dispensary for a pelvic tumor. Pre-operative diet in the hospital to improve the patient's condition did not affect the dermatitis. The removal of a large, degenerating fibromyoma was followed by the disappearance of the pellagrous manifestations without recurrent attacks. In another patient, a similar eruption, which did not respond to hospital diet, disappeared, without recurrence, following evacuation of a large pelvic abscess.

The influence of the absorption of toxins is possibly illustrated by the following example: A middle-aged white man who presented all of the cardinal symptoms of pellagra did not respond to treatment. Autopsy revealed a large cancer of the cecum with a degenerating center.

A similar example was seen in the case of an aged man with cancer of the prostate. Subsequent to the operation a bilateral, symmetrical dermatitis of the hands and elbows disappeared, but the patient died too soon to determine recurrence.

Five cases were seen associated with obstruction caused by cancer of the stomach. One patient developed pellagra following an operation for cancer of the stomach probably due to deficient absorption of food.

BLOOD OBSERVATIONS

The incidence of syphilis was somewhat lower than that seen in the average of admissions to the hospital. Only 15.13 per cent of patients revealed positive Wassermann reaction or other clinical evidence of syphilis.

The study of the blood revealed a secondary type of anemia in 73.63 per cent, while 24.21 per cent showed normal blood conditions. The average white blood count showed a slight relative lymphocytosis with 37.33 per cent showing absolute leukocytosis. Seventeen and fifteen hundredths per cent showed a marked leukopenia corresponding to Findlay's observations.[7] The blood pressure was uniformly low, with only 10.09 per cent showing normal blood pressures; 8.07 per cent with

7. Findlay, G. Marshall: The Leucocyte Changes in Pellagra Compared with Those Occurring in Beriberi, Path. & Bact. **23**:490 (Dec.) 1920.

hypertension which might be attributed to concomitant diseases and 25.22 per cent with a definite hypotension; the lowest systolic pressure being 70 mm. of mercury. Forty-two patients ran a definite subnormal temperature.

The urinalysis in the series showed 23.20 per cent to have a slight trace of albumin; 65.58 per cent were negative and 21.18 per cent were not examined.

The duration of the disease varied from two weeks to two years with the greatest number lasting two months.

Only 18 per cent of the patients had a study of the gastric secretion. Sixty per cent of these showed an hypo-acidity. In 9 per cent the spinal fluid was studied; only two showed an increase in cells or globulin.

The examination of the stool failed to reveal a higher percentage of parasites than that found in routine examination of patients in the hospital.

RESULTS

The treatment in all cases was a balanced diet with a high protein intake. Sixty-four patients improved; eight recovered without subsequent attacks and nineteen died, a mortality of 20 per cent.

The pathologic process of pellagra is not specific and is limited to the skin and mucous membranes; laboratory examinations are of little value in diagnosis.

In reviewing ten cases in this series which came to autopsy, specific changes which might be considered pathognomonic of pellagra either in the skin or in the mucous membranes were not found. The early lesions were those of inflammatory infiltration followed by atrophy. There was a marked thinning of the mucosa especially the proximal portion of the small intestine.

As to other systems involved, the only constant change was that of fatty degeneration of the liver.

MUCOUS MEMBRANES

Thirty-five and thirty-one hundredths per cent of the patients did not show any lesions of the mucous membrane. Sixty-four and fifty-seven hundredths per cent showed lesions of the mucous membrane with glossitis the most common observation; stomatitis occurred in 31.27 per cent, gingivitis in 16.14 per cent, vulvovaginitis in 12.10 per cent and proctitis in 10.09 per cent.

The pathologic process in the mucous membrane is almost as characteristic as are the lesions of the skin and has the advantage of appearing earlier with less evanescent and more permanent changes than those in the skin. The diagnosis of pellagra may be suspected and often

made on the mucous membranes alone, long before the triad of dermatitis, dementia and diarrhea appear.

The proctoscopic examination of a patient with mental depression may reveal a red, edematous rectum, with small, red puncta with the appearance of an acutely active hyperemia. Petechial spots or even small superficial ulcers may enable a diagnosis of pellagra to be made.

The tongue is more or less characteristic in acute pellagra. The fiery red edge and tip with a central brown or grayish coat is almost always indicative of pellagra. In some instances, ulceration and partial exfoliation were a part of the picture. The size or thickness is not so important. Approximately one fourth of the cases were of this acute type. In the late stage of pellagra, which is more or less characteristic, there is a definite atrophy of the mucous membrane. In chronic pellagra, the tongue is not brilliant red, but is often thick, presenting, however, a thin atrophic mucous membrane.

The buccal mucosa, involved about half as frequently as the tongue, shows the same pathologic process, but the lesions are more transient.

Chilitis occurred in seven cases. In each instance as a continuation of a stomatitis, there was exfoliation, scaling, crusting, oozing or fissuring, but characteristic diagnostic features except sharp margination and a brilliant red color were not noted.

VULVOVAGINITIS

A raw, beefy, bright red inflammation of the vagina with a pigmented or ulcerative dermatitis of the pudenda occurred in twelve patients in this series, but only twice when other mucous membranes were not definitely pellagrous. The brilliant color, which appears almost like bleeding, and the definite margin are considered diagnostic.

The appearance of the vaginal mucosa, as in all lesions of the mucous membrane, is a brilliant red, giving the impression that the blood is about to extravasate. Petechial hemorrhages are not uncommon, and a definite margin, which does not fade off as it does in the usual inflammatory conditions of the vagina, may be considered a diagnostic point in pellagra.

SKIN MANIFESTATIONS

Seventy-eight and seventy-nine hundredths per cent of the patients in the series presented skin manifestations.

While 21.18 per cent did not present manifestations of the skin, lesions of the mucous membrane and mental and gastro-intestinal symptoms were elicited.

The distribution of the skin manifestations is interesting. Fifty-seven occurred on the hands with a combination of other parts. In forty-two of the series, the eruption was seen on the elbows. This

shows that the occurrence of the dermatitis on a covered part is almost as frequent as on the exposed parts.

It is my custom to examine all areas subjected to sunlight, pressure or trauma of any character for pigmentation, such as areas over prominent spines or the sacral region. Sunlight appears as a small causative factor in the development of the dermatitis. A pellagrous necklace was seen in but a few instances.

Lesions occurred in areas not exposed to light and in ten patients treated with very small amounts of ultraviolet light, no appreciable effect was noted. Lesions appearing over the back, the elbows, the prominent spines, and the sacrum and malleoli suggest trauma or irritation as a factor in production of the dermatitis. In a number of cases, the pellagrous dermatitis was ushered in as a dermatitis venenata.

Trauma of various kinds apparently play a more important part than any specific photodynamic action in the production of lesions of the skin.[8]

The usual eruption characteristic of acute pellagra is a bilateral, symmetrical, pigmented and scaly dermatitis which is preceded by erythema, edema and inflammatory infiltration.

A bilateral distribution is, I believe, necessary for a diagnosis of pellagrous dermatitis.

The dermatitis often begins as a macular erythema which becomes confluent within a few hours. At times an erythema which presents a diffuse pinkish appearance initiates the skin symptoms. In some instances this may be followed by edema, vesiculation and even bullae formations. As these lesions resolve, browning, pigmentation and scaling occur.

There is usually a definite margin early in the disease which becomes less pronounced.

Only about one fourth of the patients in our series showed this type of eruption. The characteristics of pellagra have been aptly described by Howard Fox,[9] and the acute cases in this series have conformed to the eruption as described by him.

Ormsby [10] described the skin manifestations of pellagra fifteen years ago, and that classic description is seen in all of our earlier cases, but within the past few years, certain changes from the typical are beginning to be noted. The last stages without being able to discern the intermediate stages are now being observed. There is an increased tendency to mildness of the skin symptoms.

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8. Day, Douglas Merrill, and McIver, Monroe Anderson: Photodynamic Action of Extracts of Various Groins with Special Reference to Pellagra, Am. J. Trop. Med. **2**:115, 1922.

9. Fox, Howard: M. Rec. **70**:1910, 1910.

10. Ormsby, Oliver: South. J. Cutan. Dis. **30**:598, 1912.

The typical and bizarre dermatitis which has been considered diagnostic is rare. Roberts [11] noted the same thing in reviewing the Italian cases, and remarked that Casal's collar was fast disappearing from Italian patients who had pellagra.

A pinkish discoloration of the hands and perhaps of the face and neck is often seen with either subsequent pigmentation, tanning, or perhaps, some atrophy. Sharp margination is no longer so pronounced. The pellagrous edema, formerly so common, is seen less and less. Dermatologists are beginning to realize that pellagrous dermatitis may assume the character of a mild erythema or slight pigmentation without gross evidence of inflammatory change, and they also realize that this may or may not be followed by atrophy. Acute pellagrous dermatitis is becoming rare, and there is a tendency toward chronicity.

Not to have seen pellagra in its worst form is to have missed much, for only a small percentage of pellagrins now typify the classic description. It may be that a suspiciousness of mind enables one to discover these milder cases, or more accurate hospital records may be responsible for the realization that a patient may present mild symptoms in one or two attacks and later have the diagnosis confirmed by the development of a typhoid type of pellagra.

Pigmentation, often considered a diagnostic point, may be slight or absent. On the other hand, pigmentation without gross evidence of dermatitis is often seen. Again, a brownish discoloration of a skin showing atrophy may be the only manifestation noted.

In chronic pellagra, a dry, roughened, discolored skin, particularly over the internal and lateral malleoli, is often seen and is suggestive of the disease.

SUMMARY AND CONCLUSIONS

In 109 cases carefully reviewed, the greatest incidence of pellagra was seen among women who were either housewives or cooks.

In one instance a history of other pellagrins in the family was found.

Only 18.17 per cent came from areas which did not have modern sanitation.

Pellagra is rarely seen in patients not suffering from some previous contributory disease which disturbs metabolism.

Lesions of the mucous membrane are as important in the diagnosis as the skin manifestations.

In 8 per cent of the cases, skin manifestations disappeared following removal of some focus of absorption, suggesting that the dermatitis is a toxic dermatitis.

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11. Roberts, Stewart R.: Pellagra, St. Louis, C. B. Mosby & Company, 1912.

Trauma plays an important part in the production of lesions of the skin.

Skin manifestations in pellagra are becoming milder and more atypical.

Pellagra at one time a skin disease, diagnostically is rapidly becoming a disease which no longer depends entirely on skin manifestations.

ABSTRACT OF DISCUSSION

DR. HOWARD FOX, New York: Few of us have an opportunity to see such large numbers of patients with pellagra as has Dr. Crutchfield in Texas. My interest in this subject was first aroused by attending the congress on pellagra in 1908, in South Carolina. Shortly after this, I was able to present a patient at the Academy of Medicine, the first to be shown before a medical society in New York. Cases had been reported previously by Sherwell of New York. I am surprised to hear Dr. Crutchfield say that pellagra is so prevalent at the present time in the south. When the American Medical Association met in New Orleans a few years ago, it was almost impossible to find any cases in the Charity Hospital for presentation. Since my connection with Bellevue Hospital, I have seen several classic examples of pellagra, some as typical as the case we recently saw at Baltimore. Since 1914 thirty-seven cases have been definitely diagnosed as pellagra at Bellevue Hospital, the majority having been observed in the last few years. A great many cases have been put down as doubtful, and it is possible that the disease may be changing in character or that we may be keener in diagnosis.

In view of the fact that one of our members is to read a paper at the meeting of the American Medical Association and discuss the relationship of alcoholism in pellagra, I have looked up the records at Bellevue Hospital in regard to alcoholism and have found that in twenty cases alcoholism was noted. Fifteen patients had been heavy drinkers of whisky or gin, while five of the patients were moderate drinkers of alcohol.

DR. J. B. SHELMIRE, Dallas, Tex.: In 1907, Dr. Merrell of Albany reported the first case of pellagra in Texas. In 1908, I saw and reported the first case in Dallas. In the past ten years I have seen less and less of this disease until a recent recurrence. The day before I left Dallas I went to the City Hospital, where there are 279 beds, and there were ten classic cases of pellagra and one dead patient. I had not been attending the clinics, but my associate had been telling me of this increase. The increase has been since the meeting of the American Medical Association there last year. I was asked to get some cases of pellagra at that time, but was unable to find any that were worth presenting. My associate tells me that he has seen at least 100 cases since the first of January. Are we going to have a repetition of what we had from 1908 to 1913?

DR. PAUL A. O'LEARY, Rochester, Minn.: As a resident of the northwest, I hesitate to discuss a paper on pellagra, but for some time I have been interested in the so-called secondary type of pellagra. This form of the disease, recently called to our attention by Bender, develops secondary to a benign or malignant lesion of the gastro-intestinal tract, which prohibits the ingestion or retention of food. I have seen eight patients presenting this syndrome in the last two years and I believe the part played by the tumor is merely mechanical in that the obstruction produced leads to a faulty diet. A malfunctioning gastro-enterostomy may lead to the same circumstances. The patients who present an operable lesion have been cured of the pellagra after re-establishing an average diet following surgical intervention. It is to be borne in mind, however, that surgical procedures in the pellagrin are attended with a high mortality, and it is necessary to start the diet high in vitamin content as early as possible following the operation.

I have not observed any patients with pellagra in which the use of impure alcohol was a factor, but I can readily understand how a debauch from "canned

heat" or some other type of alcohol would lead to a dietetic insufficiency which, in turn, would produce the syndrome we call pellagra. I believe the term "secondary pellagra" must be qualified by including the predisposing factor whether it be gastric ulcer, malfunctioning gastro-enterostomy, stricture of the esophagus or impure alcohol.

Dr. Oliver S. Ormsby, Chicago: I was interested in hearing Dr. Crutchfield describe the cutaneous changes in pellagra that have taken place in the last few years. The cutaneous lesions were marked in the cases we studied in the south and in Illinois some years ago. The photosensitivity of the skin was demonstrated in our patients by having them wear fenestrated gloves and there was no question but that they developed lesions quickly in the places in which fenestrations occurred. Our experience in Illinois in regard to a great decrease in the number of cases has been the same as in other places. Fifteen years ago we had large numbers of cases, but for some time past they have been limited to scarcely enough for teaching purposes in the medical schools.

Dr. Richard L. Sutton, Kansas City, Mo.: For a long time I believe that too much emphasis has been placed on the diet as an etiologic factor in this condition. Personally, I have never been convinced of its importance. The present epidemic reported by Dr. Crutchfield would indicate that there is a much more definite factor involved than that of diet alone.

Dr. Herman Goldenberg, New York: At present there are two cases of pellagra at Mt. Sinai Hospital.

Dr. Earl D. Crutchfield, Galveston, Tex.: I wish to correct an erroneous impression. I feel that we are seeing a number of cases that do not conform to the old type, but enough of them develop to make us feel that these are probably milder cases of pellagra.

In reference to the sunlight, there is no question but what it does play a part, but I feel that it is the trauma of the sunlight rather than the light itself. Sunlight is a factor in these pellagrins, but we have felt that it was not the sunlight alone because they did not seem sensitive to small amounts of ultraviolet light.

As regards the remarks of Dr. Fox and Dr. Shelmire in reference to the amount of pellagra: some years we see many cases and the next year the disease is not so prevalent. Dr. Bedford Shelmire wrote me that he had seen at least 100 cases in their hospital recently. We have been seeing two or three cases a day, but a year ago we saw few cases. I think that the occurrence of the disease fluctuates; this year we are having more cases than usual.

URTICARIA

II. THE EXPERIMENTAL WHEAL PRODUCED ON NORMAL SKIN THROUGH INTERNAL CHANNELS *

ABRAHAM WALZER, M.D.
AND
MATTHEW WALZER, M.D.
NEW YORK

In an earlier paper on this subject,[1] we advanced a new method of production of wheals for the study of experimental urticaria. Previously, wheals had been produced only by the direct application of various agents to and into the skin. We, however, devised a method, based on an immunologic principle, by which wheals could be produced on the skin of almost any person through internal channels. It was shown that the injection of the serums of patients hypersensitive to certain food into the skin of a subject sensitized that site to the same food (Prausnitz and Küstner [2]), and that if the subject was fed the specific offending food, a wheal could be elicited at the passively sensitized site.

One of us (M. W.) has taken advantage of this technic, employing it as a means of demonstrating the absorption of certain undigested proteins from the gastro-intestinal tract. This has already been described in a preliminary communication.[3] At an even earlier date, A. F. Coca was granted permission to disclose and discuss this work, in a review of the subject of unaltered protein absorption.[4]

The histories of two hypersensitive patients who furnished the serums employed in these studies were given. The method of obtaining their blood and preparing the serum was fully discussed, and all steps and incidents relative to the complete technic for the production of such wheals were presented in detail. All experimental observations indi-

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* From the Jewish Hospital of Brooklyn, and from the Department of Bacteriology and Immunology, Division of Immunology, in Cornell University, and the New York Hospital.

* Read in abstract at the annual meeting of the Medical Society of the State of New York, Section of Dermatology and Syphilis, at Niagara Falls, N. Y., May 11, 1927.

1. Walzer, A., and Walzer, M.: Studies in Urticaria: I. Wheal Production Through Internal Channels, Am. J. M. Sc. **173**:279 (Feb.) 1927.

2. Prausnitz, C., and Küstner, H.: Studien über die Ueberempfindlichkeit, Centralbl. f. Bakteriol. **86**:160 (Aug.) 1921.

3. Walzer, M.: A Direct Method of Demonstrating the Absorption of Incompletely Digested Proteins in Normal Human Beings: A Preliminary Report, J. Immunol. **11**:249 (April) 1926.

4. Coca, A. F.: Relation of Atopic Hypersensitiveness (Hay Fever Asthma) to Anaphylaxis; a Review of the Recent Literature, Arch. Path. **1**:108 (Jan.) 1926.

cated that the offending substance gained access into the circulation in an unaltered state by way of the gastro-intestinal tract, and was carried in this form to the sensitized site. This permeability of the digestive tract to various proteins in an unaltered or undigested state has been shown in the previously mentioned communication [5] to be a normal phenomenon in a large majority of persons. As a result of the interaction between the circulating protein and the deposited reagins [6] at the passively sensitized site, the typical wheal reaction was produced. The entire question of protein absorption, with this method of wheal production as an index, is the subject of other communications soon to be published.[6a]

This method of wheal production, as has been previously noted, is ideal for the study of experimental urticaria. It is harmless, and wheals can be induced in unlimited numbers in almost any person, and at any time. It permits a detailed study of the complete unaltered reaction in all its progressive stages of development and regression. The most significant fact, however, is that it produces at will the characteristic wheal of a constitutional urticaria in a natural manner.

Lewis and Grant,[7] working independently, and evidently unaware of the publications mentioned, recently confirmed this method of the production of wheals through internal channels. They obtained serum from an adult, aged 46, markedly sensitive to fish, who was suffering from asthma, urticaria and eczema. They employed 0.5 cc. of this serum to sensitize locally a skin site on a normal subject who, eighteen hours later, was fed a whole herring. Within an hour, a wheal with pruritus and erythema appeared at the passively sensitized site.

In our studies, we found it advantageous to use much smaller quantities of material in the tests than were employed by Lewis and Grant. From 0.05 to 0.02 cc. of serum, undiluted, or in a saline dilution of 1 to 10, was the usual quantity employed. Of the foods, one egg was the amount taken for the egg serum, and one third of an average sized herring (about 50 Gm.) was ingested with the fish serum. Larger doses of serum or food caused too rapid a development of the reaction, and prevented detailed study of its progressive formation.

The object of the present communication is twofold: first, to describe the complete reaction in all its various phases as it develops on the skin

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5. Walzer and Coca (footnotes 3 and 4).

6. Coca and Grove have suggested the term reagins to designate the specifically reacting substance in the serum of hypersensitive persons. It is different from the ordinary antibodies and can best be demonstrated by the method of passive local sensitization of Prausnitz and Küstner.

6a. Walzer, M.: Studies in Absorption of Undigested Proteins in Human Beings: I. A Simple Direct Method of Studying the Absorption of Undigested Proteins, J. Immunol. **16**:143 (Sept.) 1927.

7. Lewis, T., and Grant, R. T.: Vascular Reaction of the Skin to Injury: Part VII. Notes on the Anaphylactic Skin Reaction, Heart **13**:219, 1926.

of normal persons [8] when produced with our technic; and, second, to discuss some of the factors which affect the development of the reaction.

Constitutional urticaria manifests itself, morphologically, in wheals of variable shapes, as annular, semi-annular, circinate, linear and irregularly shaped patches. They vary in size from that of a small split pea to almost any dimension; and in color they may vary from pale pink to extreme red.

We have reproduced all of these variously shaped wheals by our technic. Reactions in size measuring up to 8 cm. have been observed; and the color variations practically corresponded to those mentioned before. No particular type of wheal was characteristic of any one subject, since a number of various types occurred simultaneously on different sites on the same person. From all appearances, therefore, the wheal reactions were indentical in every respect with the clinical skin manifestations of constitutional urticaria.

The following case demonstrates the phenomenon in its consecutive stages, and illustrates a type of wheal reaction produced with our technic on the normal skin.

W. M., a nonsensitive man, on the morning of Oct. 11, 1926, was given an intracutaneous injection into the anterior surface of the left forearm (site 1) with 0.05 cc. of egg serum (K_4) taken from patient 1 of the previous report. On a corresponding site of the right forearm (site 2), a similar injection of 0.05 cc. of a nonsensitive serum was made as a control. In both instances, pinkish white elevations, about 2 to 3 mm. in size, resulted. These sites were immediately outlined with ink. Within about forty minutes, the elevations had completely flattened out. The next day, only a tiny red point, where the needle had punctured the skin, was observed at each site of injection. The subject had not taken any breakfast that day. The following are the details of the reaction recorded chronologically:

9:45 a. m.: A raw egg, well beaten, was ingested.

10:30: Pruritus was felt at site 1 (forty-five minutes after the ingestion of the egg). Nothing was felt at site 2.

10:31: A faint diffuse erythema had appeared at site 1 (one minute after onset of the reactions).

10:40: A tiny wheal had appeared at the site of injection (ten minutes after onset). The erythema and pruritus had increased.

10:56: The primary wheal had increased in size, and a number of tiny wheals had appeared around the first one. The erythema had increased in intensity and extent. The pruritus was marked.

11:00: The wheals had rapidly increased in size and number; the majority of them had joined and formed a large, irregularly shaped wheal, on which the lines of fusion were still distinguishable. Above the large main wheal were a number of tiny separate ones. The erythema was pronounced. The pruritus was intense.

8. The term "normal person," as here employed, infers a nonhypersensitive subject who does not present any obvious gastro-intestinal or skin disturbances.

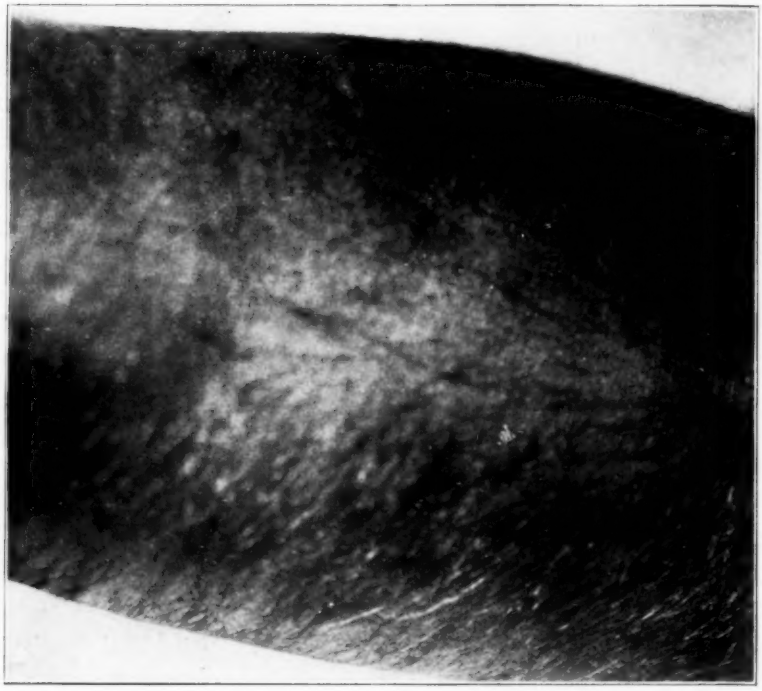

Fig. 1.—The primary wheal and a number of tiny wheals which appeared around it.

Fig. 2.—The increase in size and number of wheals, with the union of the majority of them into one large, irregularly shaped wheal. Above the main wheal are numerous small wheals.

Fig. 3.—The combination of the smaller wheals into one irregularly outlined, flat wheal.

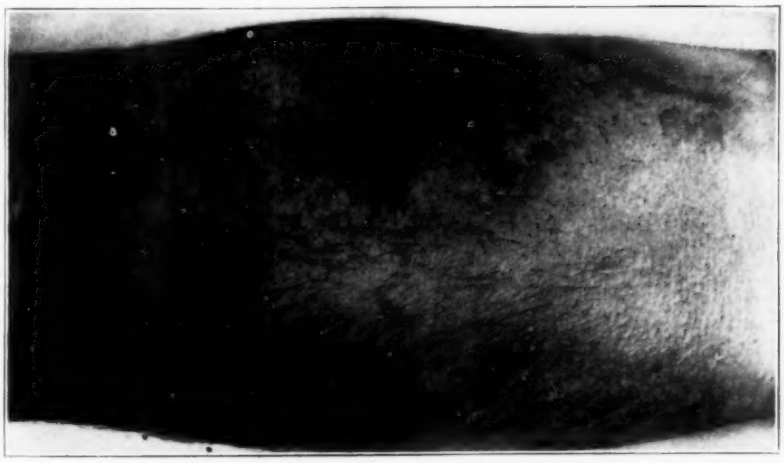

Fig. 4.—The wheal, as the sharp border was disappearing and the erythema was becoming smaller.

11 : 07 : All the wheals had combined into one large, irregularly outlined, flat wheal, including the site of injection within its borders. The erythema was pronounced and the pruritus was severe. The reaction had reached its height (thirty-seven minutes after onset). Its dimensions were 6 by 5 cm. and the wheal measured 2.5 by 4 cm.

11 : 20 : The reaction had regressed considerably. The wheal was softer and more elevated. The sharp border was almost gone. The erythema was considerably smaller, and still of a dark color. The pruritus was gone.

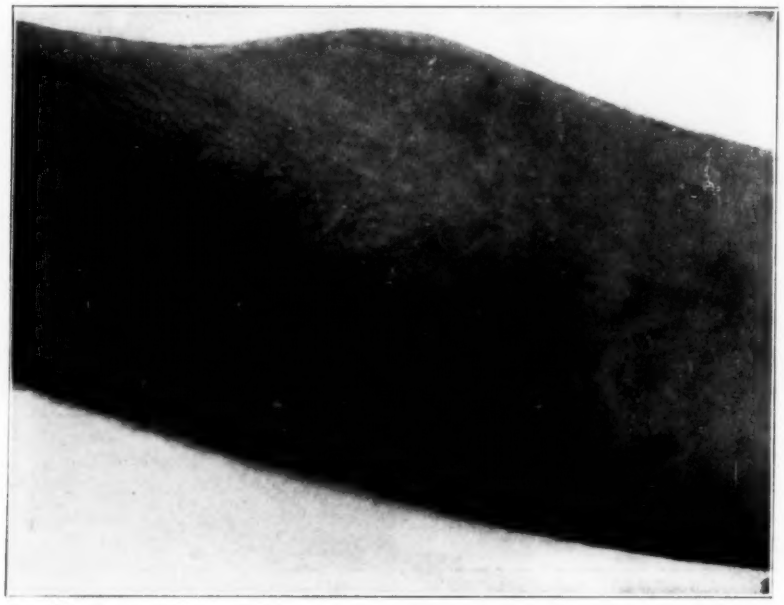

Fig. 5.—Lateral view of the wheal during regression, when the elevation was becoming soft and boggy.

11 : 28 : The reaction had rapidly diminished in size and intensity. The wheal, however, was still elevated, soft and boggy, while the borders had become indefinite. The erythema had further diminished in both size and intensity. Figure 5 demonstrates this stage of regression in a lateral view, and illustrates particularly the amount of edema.

12 : 01 : Some infiltration was still present. The erythema was limited to the sensitized site.

12 : 30 : The infiltration was gone. The erythema was still faintly visible.

4 : 25 : The erythema was gone. The site was practically normal. The reaction took five hours and fifty-five minutes. Throughout the entire time, site 2 did not show any change.

As noted in the foregoing case, the reaction presented three main characteristic features, namely, pruritus, erythema and wheal. In the typical reaction, all were present in various degrees. They did not, however, bear any constant relationship to each other, either quantitatively or in order of development. Moreover, they were not all present in every reaction. A more detailed description of each of these symptoms follows.

PRURITUS

Pruritus was usually the first manifestation of the reaction, appearing within from a few minutes to about two and one-half hours after the ingestion of the offending food. In some instances, it was absent; in others it was present only to a slight degree. Occasionally, it was the only symptom noted. This characteristic began as a gentle tickling, which increased with the gradual development of the reaction, and reached its height with the full formation of the wheal. It was usually tolerable, though in the larger and more severe reactions, it was only with extreme difficulty that the subject refrained from scratching or rubbing the site. The pruritus was, as a rule, localized to and about the site of the reaction, though in some instances it was felt temporarily a short distance away. With complete wheal formation, the pruritus was at its height, and then it gradually diminished. It was gone long before the disappearance of the erythema or the wheal.

ERYTHEMA

In the majority of reactions, the erythema followed the pruritus, though frequently it preceded or came synchronously with it. In a few instances, this symptom was altogether absent; occasionally, it was the only manifestation of the reaction.

Two distinct types of erythema were observed. Type 1 was composed of two parts: a central dark erythematous macule at the site of injection, and a more extensive surrounding erythema. Type 2 was a single uniform patch, probably as large as both parts of type 1 together.

Type 1.—This type of erythema appeared as a faint macule, which began within the site of injection and soon became uniformly dark red. It was sharply outlined, and was restricted to the site into which the serum had been injected, though occasionally it extended a trifle beyond. During the progress of the reaction, and usually before the onset of the wheal, another erythema appeared and enveloped the central macule. This associated secondary erythema began either as a faint homogeneous blush, or as a conglomeration of many closely packed fine puncta. In the latter case, as the reaction progressed, the puncta increased in number and intensity, so that it also formed a homogeneous patch. With the full development of the reaction, therefore, the secondary erythema

was one uniformly red area, more or less sharply outlined. In the center was a macule or a wheal which had either partially or completely replaced it; for, with this type of erythema, the wheal invariably developed on the macule. The secondary erythema, therefore, was always a halo for the wheal. In a number of reactions, this erythema developed even in the absence of the wheal, so that the completed reaction in such instances consisted only of the central macule and its secondary surrounding erythema, with or without pruritus.

Type 1 erythema was usually observed in slowly developing reactions, such as those which resulted either from the employment of a dilute or weak sensitizing serum, or from the absorption of small quantities of the offending food from the gastro-intestinal tract. It was less frequent in the rapidly developing or extremely marked reactions.

Type 2.—This type of erythema was a single irregularly circinate area covering and surrounding the site of injection, though the latter was not always centrally located within it. It began in one of three forms, namely, as a diffuse blush, as a group of irregularly faint macules or as a patch of closely packed fine puncta. All forms increased in size and intensity, so that at the height of the reaction, regardless of their modes of onset, one uniformly dark red patch with a sharp but irregular border resulted. At this stage, all forms were therefore identical in appearance. Anywhere within this area, irrespective of the site of injection, one or several wheals developed, for which the remaining erythema formed a halo.

After the wheals were completed, a differentiation between type 1 and type 2 erythemas could not be made; for the chief distinction between the two depended primarily on the presence of the central macule. When the wheal had completely covered this sole distinguishing characteristic, the secondary surrounding erythema of this type and the remaining erythema of type 2 were indistinguishable. Types 1 and 2 erythema could, therefore, be differentiated only at the onset of the reaction.

Type 2 was more frequently observed with the rapidly developing reactions. As with type 1, this type, with or without pruritus, was the only manifestation in many slowly forming or mild reactions. Occasionally, in such instances, the erythema did not progress any further than the three forms of onset described.

Both types of erythema completely disappeared under diascopic pressure, but reappeared when pressure was withdrawn. At the height of the reaction, the erythema usually constituted the major portion of the picture, so far as the size of the reaction was concerned. It then measured from 1 to about 8 cm. in diameter.

In many of the reactions with either type of erythema, and at the height of the wheal development, erythematous puncta appeared around the outskirts of the entire reaction. Occasionally, the puncta grouped themselves in patches, the size of peas, with intervening normal skin, and formed in annualar arrangement, like satellites on the outskirts of the erythematous area. They usually did not join with the main erythema, but persisted for a while, then gradually faded with the rest of the reaction. The appearance of these puncta, therefore, usually indicated that the reaction had reached its height.

The fading of the erythema was first noticed at the periphery, and began after the wheal had completely developed. Gradually, the erythema lost its sharp border, and became paler. It was noted that, after the subsidence of the wheal, the portion of the erythema which had been the seat of the wheal persisted the longest. Complete fading of the entire erythema in some reactions lasted as long as twelve hours from its onset, and was not followed by any desquamation.

THE WHEAL

The most striking feature of the whole phenomenon was the development of the wheal. In the majority of the reactions, it formed within the zone of erythema, and was the last of the three symptoms to appear, following the onset of the erythema by a short interval. Occasionally, it preceded or came synchronously with the pruritus or the erythema. Rarely, the wheal developed alone and, occasionally, the wheal and either the pruritus or the erythema constituted the entire reaction.

In the first paper on this subject [1] it was pointed out that, in all of the experimental work done by previous workers on urticaria, wheals formed only at the exact site where various physical, mechanical or chemical agents were applied; or only at the point where intradermal injections of various substances were introduced. Every wheal so produced, therefore, included the traumatized or injected site in its formation. This was not altogether true with the wheals produced by us. There was one type of wheal which never included the site of injection in any stage of its development. Again, the majority of the previous workers have described a definite and distinct erythema, in contradistinction to the surrounding secondary erythema, as preceding and locating the exact site of practically every one of their experimental wheals. In other words, their wheals practically always developed on an erythema that closely corresponded to that form described under type 1. This, as has been previously noted, has not been our experience.

Among the wheals produced with our technic, it was possible to differentiate two distinct types, depending on their relation to the site of injection. Type 1 wheal completely included the site of injection in

its development. Type 2 developed around, but never on, the site of injection. Type 1 could be further subdivided into three smaller groups, depending on the methods of onset and formation of the wheals.

Both types of wheals were observed to develop in the same person after the ingestion of the same offending food and use of the same serum; the individual types could not be produced at will. These variations, therefore, did not seem to depend either on the subject employed or on the quality or quantity of the offending food. Possibly, certain factors in the serum and other factors to be discussed later were responsible for the lack of uniformity in the wheal forms; for it was observed that variations were more frequent with the early supplies of egg serum than with the later. On the other hand, the fish serum gave a more uniform type of reaction, usually type 1 wheal.

TYPE 1.—*Wheals Including Site of Injection in Their Development.*

A. Wheals beginning at the site of the injection and developing therefrom.

B. Wheals beginning outside of the site of injection, but eventually including it in its complete formation.

C. Separate wheals developing both at the site of injection and outside it, eventually fusing into one wheal (a combination of forms *A* and *B*).

TYPE 2.—*Wheals not Including Site of Injection in Their Development.*

TYPE 1.—*A. Wheals Including Site of Injection in Their Development.* As has been previously stated, this was the only type of wheal produced by the early workers on experimental urticaria. While it was also the type most frequently observed by us with our technic, it was, however, not always restricted to a type 1 erythema, as was described by these previous workers. It was as frequently observed with one type of erythema as it was with the other.

This form of wheal began at the site of injection and gradually increased in size by extending peripherally. If the wheal developed on an erythema of the type 1, it was not always limited in its growth by the border of the central macule. It occasionally extended into the surrounding erythema, so that the completed wheal was larger than the macule on which it developed.

With type 2 erythema, the wheal also formed at the site of injection, and often extended beyond it; but it never completely covered the entire erythematous area.

The following case illustrates this type of wheal on type 1 erythema.

Case Illustrating Type 1 A, Wheal on Type 1 Erythema.—R. S., a nonsensitive woman, on the morning of March 16, 1927, was given an intracutaneous injection into the anterior surface of the left forearm (site 1) with 0.05 cc. of fish serum (M_3) taken from patient 2 of the previous report.[1] On a

corresponding site of the right forearm (site 2), 0.05 cc. of a nonsensitive serum was similarly injected as a control. In both instances, pinkish white elevations about 0.5 cm. in diameter resulted. These sites of injection were immediately outlined with ink. Within about thirty minutes, the elevations had completely flattened out. The next day, an erythema was observed within the site of injection 1. On March 18, two days after the injection, the erythema was gone; only a red point was noted at each site where the needle had pierced the skin. The patient had not taken any breakfast that day. The following are the details of the reaction recorded chronologically:

9:17 a. m.: One third of an average sized herring (about 50 Gm.) was ingested.

9:26: A slight itch was felt at site 1 (nine minutes after the ingestion of the fish). Site 2 was normal.

9:27: A faint erythema was observed around the point of injection (one minute after onset of the reaction). The pruritus had increased (fig. 6, *A*).

9:28: The erythema had increased in intensity and extent and covered the site of injection. The pruritus was more marked.

9:29: A small wheal had appeared on the central macular erythema, at the site of injection (three minutes after the onset of the reaction). A surrounding diffuse secondary blush or erythema was just faintly visible. The pruritus had increased (fig. 6, *B*).

9:31: The wheal had increased in size and involved the entire central erythematous macule. The surrounding erythema was darker, and had extended. The pruritus was pronounced (fig. 6, *C*).

9:47: The wheal had extended beyond the erythematous macule into the surrounding erythema, which had become darker. The pruritus was pronounced. The reaction was at its height (twenty-one minutes after the onset). It measured 6.5 by 6.5 cm. and the wheal was 2 by 1.5 cm. Tiny puncta had formed around the whole reaction. Site 2 was normal (fig. 6, *D*).

10:00: The wheal had lost some of its induration, and its borders were flatter. The erythema and puncta had decreased in both quantity and intensity.

10:08: The wheal, though it had appeared larger, was softer and bulging. The erythema had decreased in extent and in intensity. The erythematous puncta were gone. The pruritus was decreased (fig. 6, *E*).

10:14: The pruritus had disappeared. The reaction was fading rapidly.

10:20: The wheal was flat, but some of the induration still persisted. The erythema was still visible only at the site of injection.

12:30: The erythema and the induration were gone. The whole reaction took three hours and four minutes. During the entire time, site 2 had remained unchanged.

TYPE 1.—*B. Wheals Beginning Outside Site of Injection, But Eventually Including It in Its Formation.*—In this group, the wheals first appeared either as single tiny elevations or as a group of such lesions, about 1 cm. or more from the site of injection on type 2 ery-

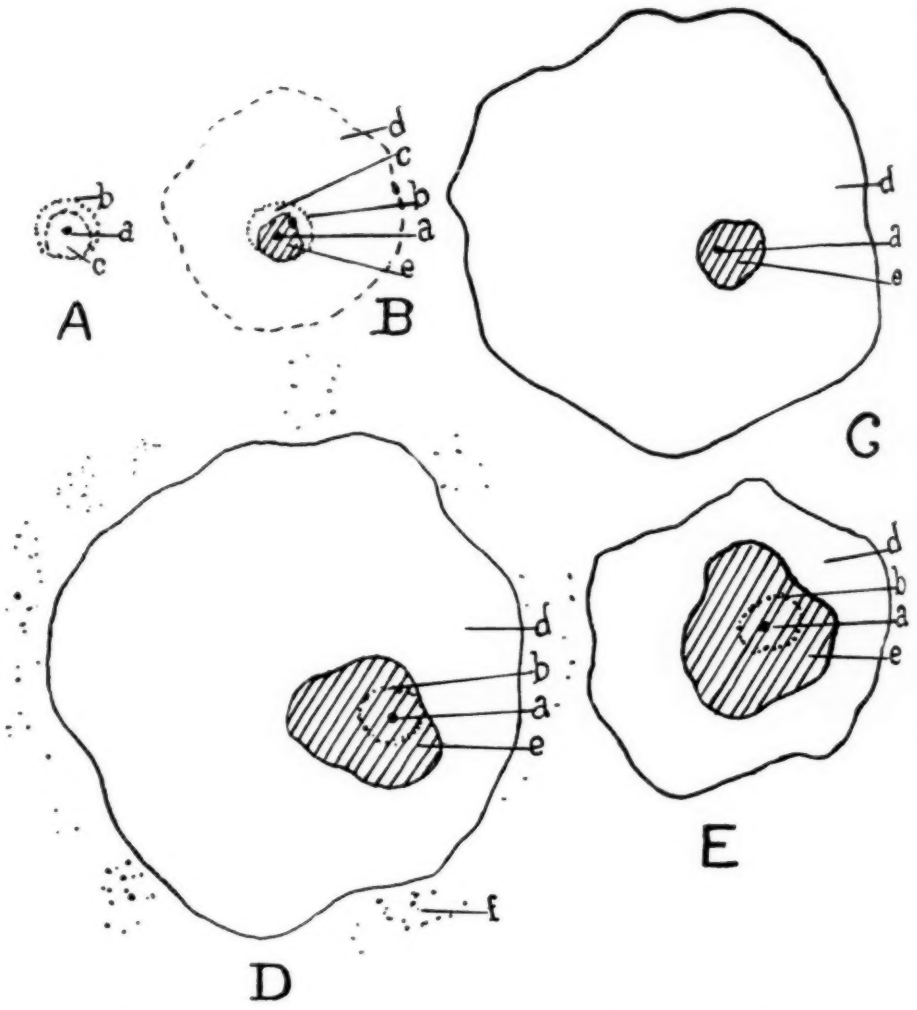

Fig. 6 (case 2, site 1).—Type 1 *A* wheal on type 1 erythema. *A* shows the faint erythema ten minutes after the ingestion of fish, the article of food to which the subject had been locally sensitized; *B*, twelve minutes after eating; *C*, fourteen minutes after eating; *D*, thirty minutes after eating, at the height of the reaction, and *E*, fifty-one minutes after eating, when the reaction was decreasing. *a* indicates the point at which the serum had been injected; *b*, the outline of site of injection; *c*, macular erythema; *d*, secondary blush or erythema; *e*, wheal, and *f*, erythematous puncta.

thema. They developed either in an annular formation around the site of injection, or in a group to one side. With the completion of the reaction, however, a single wheal was the usual result, with the site of injection included within it. In rare instances, one or two of the tiny wheals never fused with the rest. This type of wheal formation is well illustrated by the following case.

Case Illustrating Type 1 B Wheal on Type 2 Erythema.—A. S., a man, aged 34, was given an intracutaneous injection into the right forearm (site 1) with 0.05 cc. of undiluted egg serum (K_4) at 2:10 p. m. on Aug. 20, 1925. On a corresponding site in the left forearm (site 2) 0.05 cc. of a nonsensitive serum was injected similarly as a control. On August 21, the appearance of the site of injection was normal. The patient had coffee and toast at 8 a. m. on the day of testing. He did not have any lunch, but at 2:20 p. m. had an egg in malted milk. The results were as follows:

2:20 p. m.: One egg in a glass of malted milk was ingested.

3:55: Pruritus with a patch of erythematous puncta began at site 1 (one hour and thirty-five minutes after the ingestion of the egg).

4:00: A small wheal appeared close to site 1 (five minutes after the onset of the reaction). The puncta had increased in number and intensity and formed one uniform patch of erythema. Site 2 was normal (fig. 7, *A*).

4:05: The wheal had increased in size, and included the site of injection in its formation. The erythema was more marked and had extended. The pruritus had increased.

4:14: The wheal had enlarged, and the erythema was more pronounced. The pruritus was more marked (fig. 7, *B*).

4:19: The wheal had increased in size, and new wheals had sprung up at the upper border. The erythema and pruritus were more marked.

4:28: All the wheals had combined into one. The result was a pronounced, elevated, hard, almost white wheal, with a projection at the upper border. The erythema was dark red, and the pruritus was quite marked. The reaction had reached its height (thirty-three minutes after the onset). It measured 6 cm. by 6 cm. and the wheal was 2.5 cm. by 2.75 cm. Site 2 was normal (fig. 7, *C*).

4:35: The wheal had softened and diffused. The erythema was pronounced, and of a deep red color. The pruritus was still quite pronounced.

4:45: The process of recession continued. The wheal, erythema, and pruritus had diminished.

5:00: The wheal was much smaller, the erythema was fainter. The pruritus had gone.

5:50: The infiltration was gone. The erythema, though still present, was smaller and fainter, and only occupied the site of injection.

7:30: The erythema was still faintly visible.

8:30: The erythema was gone. Throughout the entire time, site 2 was normal. The entire reaction took four hours and thirty-five minutes.

TYPE 1.—*C. Separate Wheals Developing Both at Site of Injection and Outside It, and Eventually Fusing Into One Wheal.*—This form of wheal was practically a combination of the two preceding ones, and occurred on either type of erythema. A wheal formed at the site of injection about the same time that a group of tiny wheals appeared either around or to one side of it. They all increased in size and then

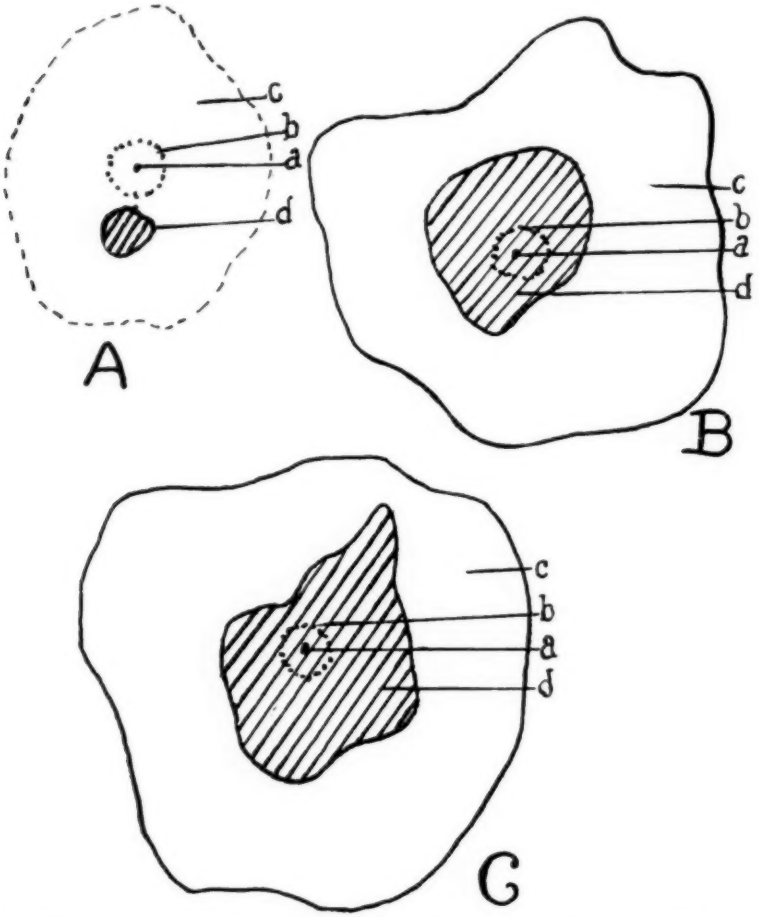

Fig. 7 (case 3, site 1).—Type 1 *B* wheal on type 2 erythema. *A* shows the wheal forty minutes after the ingestion of egg, the food to which the subject had been locally sensitized; *B*, fifty-four minutes after eating, and *C*, sixty-eight minutes after eating, at the height of the reaction. *a* indicates point at which serum had been injected; *b*, outline of site of injection; *c*, erythema, and *d*, wheal.

fused. As a rule, one large wheal, with the site of injection included within its borders, was the final result. Occasionally, however, as already observed in group *B*, one or two of these original tiny wheals never joined with the main one. The following case illustrates this type of wheal formation.

Case Illustrating Type 1 C Wheal on Type 2 Erythema.—A. W., a man, aged 40, was given an intracutaneous injection into the right arm (site 1) with 0.05 cc. of undiluted egg serum (K_4) at 9 p. m. on Aug. 5, 1925. On a corresponding site on the left arm (site 2) 0.05 cc. of a nonsensitive serum was similarly injected as a control. On August 6, the appearance of the site of injection was normal, and food was not eaten on this day. The results of the testing were as follows:

7:30 a. m.: A raw egg well beaten was ingested.

8:00: A slight itch was felt at site 1, followed almost immediately by a faint diffuse erythema (thirty minutes after the ingestion of the egg). Nothing was felt at site 2.

8:10: The erythema had increased in extent and intensity. The pruritus was more marked.

8:11: A tinty elevation appeared at the site of injection within the center of the erythema (eleven minutes after the onset of the reaction). The erythema and pruritus became more marked. Site 2 was normal.

8:13: Tiny elevated lesions sprang up within the erythema, and surrounded the central wheal, which had increased in size.

8:15: The whole reaction now consisted of an erythematous patch about the size of a fifty cent piece, with a fairly sharp border. In the center was a wheal the size of a pea completely covering the site of injection and surrounded by many tiny wheals the size of a pinhead. The pruritus was pronounced. Site 2 was normal (fig. 8, *A*).

8:18: All the peripheral wheals had rapidly increased in size and number, and fused into one large annular wheal, which encircled the central wheal at the site of injection. The lines of fusion of the smaller wheals were visible on the large annular wheal. The central wheal which had increased in size was separated from the annular wheal by a distinct complete annual depression or groove. Three tiny wheals had developed around the annular wheal. The erythema had extended and was darker. The pruritus was marked (fig. 8, *B*).

8:30: The reaction was at its height (30 minutes after onset). It was a sharp clean-cut patch with a distinct border. The wheal was bright red with a paler center, markedly indurated, and a sharp, abrupt border. On diascopic pressure, an ivory-white color showed. The erythema was dark. The pruritus was intense. The entire reaction measured 8 by 5.5 cm. and the wheal was 4 by 3.5 cm. Site 2 did not show any change (fig. 8, *C*).

8:45: The wheal had lost its sharp border and had spread a little. It was somewhat more elevated, but softer. The erythema was pronounced. The pruritus had diminished.

9:33: The wheal and erythema had diminished. The pruitus was gone.

10:30: The infiltration was still palpable, and the erythema, though fainter, was still present, as a diffuse irregular area.

3:00 p. m.: The infiltration was gone. A faint central erythema was still present.

3:25: The erythema had disappeared. A faint brownish pigmentation around the site of injection was all that was visible. The whole reaction lasted seven hours and twenty-five minutes. Site 2 had remained normal throughout.

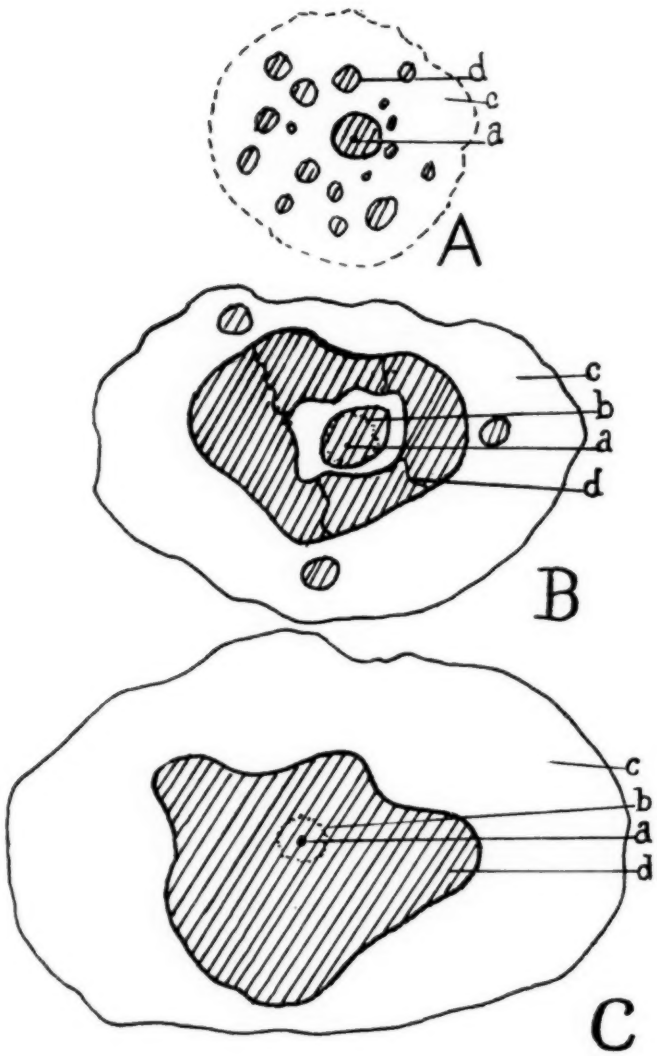

Fig. 8 (case 4, site 1).—Type 1 *C* wheal on type 2 erythema. *A*, forty-five minutes after the eating of an egg, the food to which the subject had been locally sensitized; *B*, forty-eight minutes after eating, and *C*, one hour after eating, at the height of the reaction. *a* indicates point at which serum had been injected; *b*, outline of site of injection; *c*, erythema, and *d*, wheal.

It will be noted from the preceding discussion and the cases quoted, that this subdivision of wheals is based on their early development or mode of onset. Once these wheals had reached their full development, this means of classification was lost, and their differentiation became impossible. The end-results of all of these types of wheals, therefore, were alike.

TYPE 2.—*Wheals Not Including Site of Injection in Their Development.*—This type of wheal was probably the most unusual of all, since the site at which the specific serum had been injected never took part in its formation. It developed as follows: Either one or a number of tiny elevated lesions appeared about 1 cm. or more from the site of injection, on a type 2 erythema, and rapidly increased in size. If many were present, they soon fused, forming usually one semi-annular, or irregularly shaped annular, wheal around, but never including, the site of injection. As in form *B* and *C* of type 1, some of the original wheals often failed to unite with the others. The following case illustrates this type.

Case Illustrating Type 2 Wheal on Type 2 Erythema.—W. A., a man, aged 42, was given an intracutaneous injection into the right forearm (site 1) with 0.05 of undiluted egg serum (K_2) at 1 p. m. on Sept. 5, 1925. On a corresponding site on the left forearm (site 2) 0.05 cc. of a nonsensitive serum was similarly injected as a control. On September 6, the appearance of the site of injection was normal, and food was not taken until the test was conducted. The results of the testing were as follows:

8:05 a. m.: A raw egg well beaten was ingested.

8:35: A slight itch was felt a short distance above site 1 (thirty minutes after partaking of the egg). Nothing was felt at site 2.

8:45: A group of small erythematous macules appeared at the same location (ten minutes after the onset of the reaction), but site 2 did not show any changes.

8:48: The erythematous macules had increased in size, joined and extended downward, embracing the site of injection, and two tiny wheals had appeared within it (thirteen minutes after the onset of the reaction). The pruritus was pronounced. Site 2 was normal.

8:50: The wheals had increased both in number and in size. The erythema had become darker and more sharply outlined. The pruritus was more marked (fig. 9, *A*).

8:55: The wheals had increased in size and were chiefly located above the site of injection, though some were below. The erythema was marked, the pruritus had increased.

9:05: The wheals, which had rapidly increased in size, conglomerated into three — two above the site of injection, and one below and to one side of it. The erythema had increased in size and in intensity. The pruritus was marked. Site 2 was normal (fig. 9, *B*).

9:08: The wheals had rapidly increased and combined into one patch of semi-annular shape. A tiny wheal had appeared on either side. The main wheal stood out prominently, with sharp borders. The

infiltration was marked. The erythema and pruritus were pronounced (fig. 9, *C*).

9 : 14 : The wheal was prominent and pink, with a paler center. The infiltration was marked, almost board-like. The tiny wheals had increased in size. The erythema was dark red with a sharp but irregular border. The pruritus was severe.

9 : 25 : All the wheals had combined into one, but the site of injection was not included in its formation. The erythema was pronounced, but the pruritus was not as intense as previously. This was the height of the reaction (thirty minutes after onset). It measured 5 by 7 cm. and the wheal measured 1.5 by 5 cm. (fig. 9, *D*).

9 : 35 : The wheal had spread, the borders were flatter, and the infiltration was not as greatly marked as before. The erythema had lost its sharp border, and there was considerably less pruritus.

9 : 41 : The wheal was softer, and it shaded off into the surrounding erythema, which was fainter. The pruritus was slight.

10 : 05 : The infiltration was still present, the erythema had almost completely faded and the pruritus was gone.

12 : 00 : The entire reaction was gone. It took three hours and twenty-five minutes. Site *2* was normal throughout.

Irrespective of the type or form of the reaction, the primary wheal was a faint pink, elevated, sharply circumscribed, infiltrated lesion, the size of a pinhead, and with a smooth surface. It rapidly increased in extent, elevation and infiltration. If a number of such wheals developed in the course of the reaction, the adjacent ones often conglomerated, so that usually one wheal was the result, without any evidence of the fusion of the smaller lesions. It reached its height of development within from a few minutes to about an hour from the onset of the reaction. The size of the completed wheals varied from a few millimeters to about 6 cm. It was firm to the touch, smooth, round or irregularly oval, semi-annular or annular in contour, with or without pseudopods. It varied from pink to red, with a somewhat paler center. The wheal was elevated, in some instances about 2 to 3 mm. above the surrounding skin, with a sharp and almost perpendicular border. On diascopic pressure, an ivory-white color showed.

Having reached its full development, the wheal was stationary for a minute or two, and then slowly began to recede. Spreading of the sharp perpendicular border was noted, which first gave the impression that the wheal was increasing in size rather than subsiding. Closer observation, however, showed that the hard infiltrated edema so characteristic of the original wheal was gone, and that the fluid of the wheal diffused into the surrounding tissues, producing the apparent increase in size. This release of tension of the fluid of the wheal, therefore, was a positive indication that it had passed its height. Bulging and softening, with a tendency to pitting, was then noted. With the gradual absorption of the

fluid, the flattening of the wheal followed. This whole process of regression usually took from a few minutes to several hours. Desquamation of the skin was not observed after complete subsidence of the reaction. After the extremely marked reactions, a faint brownish pigmentation was occasionally noted at the sites on the following day.

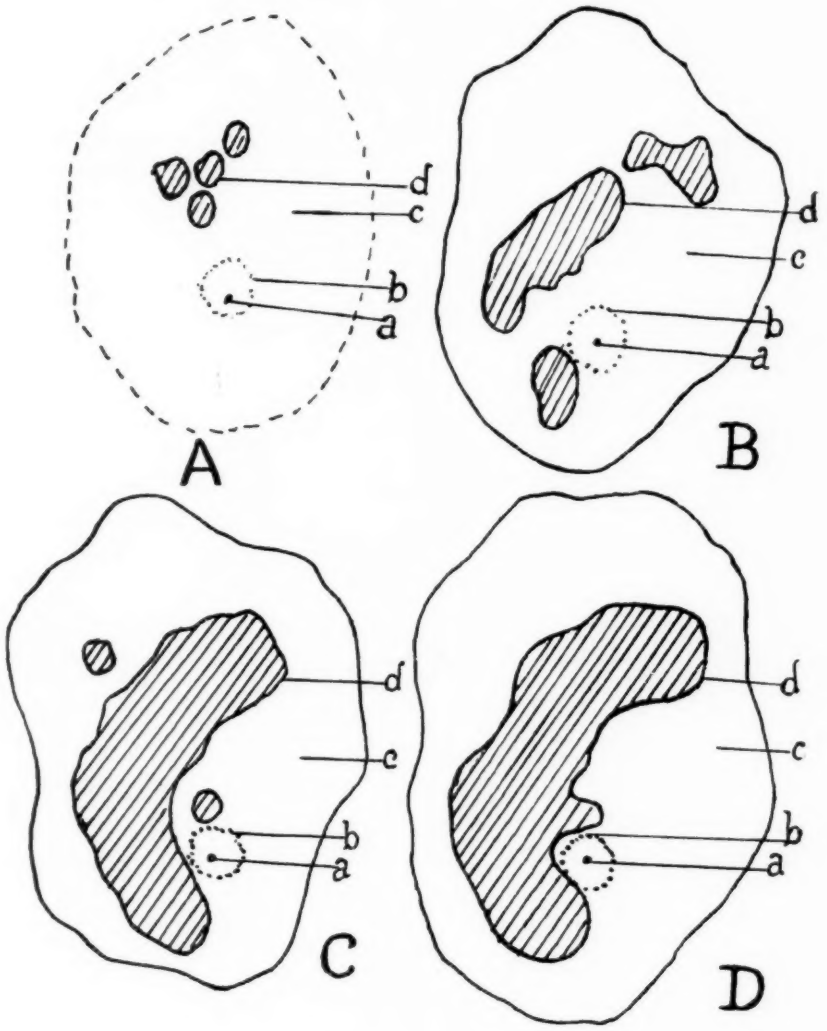

Fig. 9 (case 4, site 1).—Type 2 wheal on type 2 erythema. *A* shows wheal forty-five minutes after eating an egg, the food to which the subject had been locally sensitized; *B*, one hour after eating; *C*, one hour and three minutes after eating, and *D*, one hour and twenty minutes after eating, at the height of the reaction. *a* indicates point at which serum had been injected; *b*, outline of site of injection; *c*, erythema, and *d*, wheal.

REACTIONS FOLLOWING TRAUMA TO THE SITES OF A PREVIOUS WHEAL

Traumatizing the sites of the skin that had been the seats of marked reactions produced some unusual phenomena. If on the day following a severe reaction, certain forms of external mechanical irritation, as rubbing or scratching, were applied to such sites, another definite local reaction could often be elicited. This response was in the form of a pruritus, usually accompanied by an erythema, and occasionally also with a wheal. These reactions were not particularly active, however, and were neither as pronounced nor as prolonged as the original ones. In some instances, they could be induced repeatedly at the same site by similar irritation, but all successive reactions were correspondingly milder. Such phenomena could not be produced on a sensitized site previous to the original reaction by the production of a wheal.

The dermographic response of these sites was also frequently altered. With firm stroking across the site of the previous wheal, the usual red line formed in the direction of the trauma. Within a few minutes, in some instances, this line widened, and a faint pinkish white edematous ridge developed down its center. This was the usual dermographism as it is frequently observed in various degrees in many persons. The unusual feature of the reaction as noted here, however, was that within the area of the previous wheal the line of demographism persisted for a long time after the rest of the line on the normal skin had disappeared. In other words, some change had taken place within this area of skin, which increased the intensity of the dermographic reaction and prolonged it beyond its normal limit. This alteration in dermographic response was due to changes resulting from the wheal reaction; for, previous to it, the dermographic reaction on the sensitized site was the same as elsewhere on that subject.

While the foregoing phenomena resulting from these various forms of trauma have been repeatedly noted, they could be produced only on some of the sites that had been the seats of marked wheal reactions. They were most frequently observed following the use of the early specimens of the egg serum, freshly obtained at the beginning of this work.

FACTORS WHICH AFFECT THE DEVELOPMENT OF THE REACTION

During the course of the present studies, it was noted that modifications of the usual types of reaction in size, intensity, rapidity of development, form, etc., frequently occurred. These were dependent on a number of factors, the most important of which may be tabulated as follows:

I. Factors affecting local sensitization of the site.

A. Qualitative and quantitative properties of the sensitizing serum.

B. Ability of the subject to accept passive local sensitization.
C. Location of the sensitized site on the subject.

II. Factors influencing the absorption of the offending proteins.
A. Food.
B. Factors pertaining to the permeability of the gastro-intestinal tract.

III. Factors concerned with variations in technic.
A. External trauma.
B. Repetition of the reaction in the same sensitized site.
C. Injection of the serum subsequent to the ingestion of the offending food.

I. *Factors Affecting Local Sensitization of the Site.—A.* Qualitative and quantitative properties of the sensitizing serum. The degree of the reaction depended to a great extent on the amount of the reagins of the sensitizing serum which were anchored at the sensitized site. It was therefore the strength, or reagin content of the serum which often determined the size and intensity of the reaction. The amount of reagins not only varied with the different serums, but was commonly observed to vary in the serum of the same patient when taken at different intervals.

The serum retained its activity when kept under proper conditions for a long time; its aging, nevertheless, greatly diminished its power of wheal induction. This loss of potency, however, was gradual, and only became apparent after several months. Reactions have been obtained with serum from six to fifteen months old; but, in comparison to the original reactions, they were considerably diminished in size, intensity or rapidity of development. The diminution in amount and severity of the pruritus was especially noticeable with the old serums.

Dilutions of the serum correspondingly diminished the reaction, and were employed only when less active reactions were desired. The highest dilution with which a reaction was elicited was 1:640. The usual strength employed in the present series of tests was either whole serum or a saline dilution of 1:10.

The quantity of the serum injected, though apparently less important than its dilution, was another factor that influenced the degree of the reaction. About 0.05 to 0.025 cc. was the amount usually employed. Larger or smaller quantities correspondingly affected the reaction, though not in direct proportion to the amount injected.

B. Ability of the subject to accept passive local sensitization. Coca and Grove,[9] working chiefly with pollen serums, found that 11 per cent of 103 persons failed to accept passive local sensitization. In other words, it would seem that only 89 per cent of the subjects would accept local passive transfer of sensitivity and could be employed in the experimental production of wheals through internal channels with the technic

9. Coca, A. F., and Grove, E. F.: Studies in Hypersensitiveness: XIII. A Study of the Atopic Reagins, J. Immunol. **10**:445 (March) 1925.

here described. Brunner and Walzer,[10] however, in their studies of the absorption of undigested fish protein, employing the same fish serum and technic used by us, found in their first sixty-four cases not an instance of failure to accept passive local sensitization. Sussman, Davidson and Walzer,[11] and Wilson and Walzer,[12] in studies of the absorption of undigested egg protein in more than 100 adults and children obtained similar results with our serum and technic. It can therefore be definitely concluded that, with the fish and egg serums employed in these studies, failure to accept passive local sensitization is a negligible factor. There have been, however, occasional instances in which passive local sensitization had failed to occur. In this connection, it is of interest to note that two of the patients from whom the present fish and egg serums were obtained could not be sensitized with each other's serum. These patients, however, were abnormal in that they themselves were extremely hypersensitive to certain foods. This entire subject, which is of importance from an immunologic point of view, will be discussed in a future communication.

C. Location of the sensitized site on the subject. The reaction has been produced on almost every part of the body: arms, forearms, back of the hands, chest, back, abdomen, thighs and legs. The face was never utilized for this purpose. Practically all the locations, with the exception of the forearms and the back of the hands, responded equally, both as to time and size of the wheal. The forearms and the back of the hands repeatedly showed delayed reactions of a few minutes, and the wheals were often smaller than the controls on other parts of the body. This confirms the previous observations of Brunner and Walzer.[10] The arms were the usual sites chosen for all tests, for obvious reasons. For certain studies, the forearms were employed for convenience, in spite of their delayed and diminished reactions.

II. *Factors Influencing the Absorption of the Offending Protein.*—*A.* Food. The quantity of the offending food ingested affected the degree of the reaction. With the serum sensitive to eggs, one egg was usually taken; and with the serum sensitive to fish, about 50 Gm., or one third of an average sized herring was ingested. If the amount was increased or diminished, the reaction varied, accordingly.

To produce the best results, the foods had to be taken in their natural state. Heating, baking, canning, etc., diminished, delayed or prevented the reaction.

B. Factors pertaining to the permeability of the gastro-intestinal tract. In the unpublished experiments of Brunner, Sussman, Davidson,

10. Brunner, M., and Walzer, M.: To be published.
11. Sussman, H.; Davidson, A., and Walzer, M.: To be published.
12. Wilson, S. J., and Walzer, M.: To be published.

Wilson and Walzer mentioned previously, it was found that, following the oral administration of fish and egg to adults, 93 per cent of one series absorbed sufficient unaltered fish protein, and 85 per cent of another series absorbed sufficient unaltered egg protein to cause a reaction. In infants and children, the permeability to egg protein was slightly less than in adults. These studies, therefore, seemed to indicate that the enteral tract was slightly more permeable to fish than to egg. This was further supported by the fact that the onset of the fish reaction usually occurred in from one to seventy-five minutes, with an average of seventeen minutes, while the egg reaction took from twenty-five to 105 minutes with an average of about fifty-four minutes.

It was also noted by these workers, and was corroborated by us, that the presence of food in the stomach, preceding the ingestion of the offending protein, was an important factor in retarding, diminishing or preventing the local response at the sensitized site. Hyperchlorhydria and organic diseases with which it is associated such as gastric and duodenal ulcer, tend to retard or prevent the reaction. Achlorhydria and the administration of alkalis, on the other hand, tend to accelerate it.

III. *Factors Concerned with Variations in Technic.—A.* External trauma. Any external mechanical irritation, in the form of scratching, rubbing, brushing, pinching, etc., applied to the sensitized site during the development of the reaction, accelerated the formation of the wheal, and increased the intensity of the local response.

B. Repetition of the reaction in the same sensitized site. A passively sensitized site usually retained its sensitivity for a number of weeks, provided the offending food was not eaten. The production of a marked reaction by the first ingestion of that food, as a rule, completely neutralized the deposited reagins at that site. Often, following the milder reactions, wheals could be reproduced at the same site a number of times, by repeating the ingestion of the same food. The primary wheal was usually the largest and most active.

Occasionally the initial reaction was small, owing to lapses in technic such as the feeding of the offending food on a nonfasting stomach. In such a case, repetition of the test under corrected conditions elicited another reaction at the same site, larger than the primary one. With the employment of the routine technic, however, successive reactions were correspondingly smaller and less active than the previous ones. The pruritus was neither as pronounced nor as prolonged. The erythema assumed either type, and occasionally was the only manifestation of the reaction. Both types of wheals were observed, though possibly type 2 was slightly more frequent.

C. Injection of the serum subsequent to the ingestion of the offending food. The usual method of wheal production was, as has been

previously stated, that of passively sensitizing a site in a subject, and later feeding him the offending food. In reversing the order, that is, injecting the specific serum after the subject had partaken of the offending food a short time previous, a wheal could still be produced at the site of injection. These reactions followed in from five to sixty minutes, and were smaller and less active than those produced by the usual method. The largest and most active reaction occurred from four to six hours after the ingestion of the food; in other words, at that time the offending protein was at its highest concentration in the circulation. This method of wheal production was adopted in the studies of protein absorption, which will be discussed by us in another communication.

COMMENT

The reactions just described simulate clinically and morphologically the pathognomonic manifestation of urticaria. Practically all the cutaneous symptoms which have been observed in constitutional urticaria have been reproduced: pruritus, from a slight to an almost unbearable itch; erythema with all its modifications in form, size, color and intensity, and the wheal with its variations in form, color, elevation, induration, border and pseudopods. Any of these, occurring alone or in association with the others, is as characteristic in this reaction as it is in constitutional urticarias.

As has been previously stated, the most significant feature of the whole reaction was the variety of wheals observed. Exclusive of type 1 *A*, all forms here described were never produced by the previous workers on experimental urticaria. Probably the most unusual wheal was type 2, the one which never included the site of injection in its formation. The only wheal mentioned in the literature which bears any resemblance morphologically to it is the "miniature crater wheal" described by Lewis and Grant.[13] This wheal is of external origin, produced by histamine, punctured into the skin, the development of which is affected by mechanical factors. Lewis and Grant describe the production of this wheal as follows: A sphygmomanometer cuff is placed on the upper part of the arm and the pressure in it is raised to a point far above the systolic pressure.

> Histamine is punctured into the occluded arm, which is subsequently heated . . . . if this occlusion and heating is sufficiently prolonged, no wheal appears. If less prolonged, a miniature crater develops; that is to say, while no wheal develops in the immediate neighborhood of the puncture, a minute ring of edema appears around the central point and at a radial distance of about 2 millimeters or a little more.

13. Lewis, T., and Grant, R. T.: Vascular Reaction of the Skin to Injury: Part II, Heart **11**:209 (May) 1924.

They explain this reaction as follows:

> This phenomenon is due to the interplay of two events, refractoriness of the tissue and diffusion of the poison. The histamine is put down centrally and spreads radially and gradually. The tissues near the center, during the period of occlusion, are longer in contact with the histamine than are those into which diffusion eventually occurs. The vessels of the central portions lose their permeability and become refractory, while histamine is still spreading into fresh tissue at the margin. If, at this stage, the circulation is released, whealing occurs in the form of the minute border ring described.

Lewis,[14] in a further discussion along this line, says that "a variety of injuries which produce dilatation and increased permeability of the vessels of the skin leave these vessels temporarily in a curious state . . . they are refractory, relatively or absolutely . . . to a second injury, whether of the original or of a different kind." According to these workers, therefore, refractoriness of tissue implies an inability to respond with a wheal formation through "a decline of a previously increased permeability" of the cells of the capillaries.

Such refractoriness of the site of injection cannot be applied as a plausible explanation for the formation of the type 2 wheal; for there is no evidence that the site of the type 2 wheal had been the seat of any increased permeability or any alteration resulting from the sensitizing injection to which the site of type 1 wheal had not been similarly subjected. Moreover, diffusion of the sensitizing serum into the surrounding tissues, while it may occur to a certain degree in any intradermal injection, might explain the formation of the wheal peripherally; but it does not account for the absence of the wheal at the site of injection. This certainly cannot be due to the absence of reagins at this site, as direct intradermal testing with the specific offending protein invariably resulted in a wheal at the site of injection. It is rather significant that, in the thousands of skin tests made by Walzer and Kramer [15] on passively sensitized sites, according to their technic of indirect testing for hypersensitiveness, type 1 wheal alone always resulted, and type 2 was never encountered. In the hundreds of intradermal tests made by us on sites passively sensitized with the same fish and egg serums employed in the present studies, type 2 wheal was never observed. It was induced only by the constitutional administration of the offending substance.

Moreover, if refractoriness were to be accepted as the basis for the mechanism of type 2 wheal, all wheals recurring at the site of a previous type 1 wheal would be expected to be of type 2. This, however, was

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14. Lewis, T.: Vascular Reaction of the Skin to Injury: Part IV, Heart **13**:153, 1926.

15. Walzer, M., and Kramer, S. D.: Studies in Specific Hypersensitiveness: XVIII. An Indirect Method of Testing for Conditions of Atopic Hypersensitiveness (a Preliminary Report), J. Immunol. **10**:835 (Sept.) 1925.

not the case; and, while type 2 wheals might have been slightly more frequent under these conditions, type 1 wheals occurred entirely too often to be disregarded. It is obvious, therefore, that there must be factors involved in the mechanism of formation of type 2 wheals other than those offered by Lewis and Grant for the explanation of their crater wheal. What these factors are is still a subject of investigation. It may well be that some sort of refractoriness does exist at some of the sites of injection which is responsible for the formation of type 2 wheal; but it is apparent that the refractoriness, as outlined by Lewis and his co-workers, and supported by Hare,[16] is as yet insufficient to explain this phenomenon.

It is probable that the variations between the wheals described by us and those produced by all previous workers are the result of the fundamental differences in the technic of their production; for it is to be recalled that all previous workers produced their wheals by local measures, whereas we produced ours by constitutional means. The fact that the offending protein reaches the sensitized site through the circulation definitely distinguishes the mechanism of these types of wheals from those previously produced; and this, together with the certain possible inherent properties of the serum, may be responsible for type 2 wheal.[17] It is certain, whatever the explanation for them may be, that the offending food, subjects employed and skin sites can all be ruled out as specific causes.

Another distinguishing feature which characterizes the type 2 wheal is the fact that it is not the outgrowth of a central lesion which has progressively enlarged radially and subsided in the center. It appeared originally as an annular or semi-annular lesion, or formed from the fusion of numerous small elevated lesions around the site of injection. In this connection, it is of interest to note a similarity between the development of this type of wheal and that not infrequently observed in certain forms of urticaria. This is especially true in giant urticaria, in which large annular or semi-annular wheals are frequently seen, which did not develop as a radial expansion of central elevated lesions,

16. Hare, R.: An Experimental Investigation Into the Vascular Reaction of the Susceptible Skin to Protein, Heart **13**:227, 1926.

17. Gay, L. N., and Chant, E. The Passive Transfer of Hypersensitiveness (Local and Contralateral Passive Transfer Experiments) Bull. Johns Hopkins Hosp. **40**:270 (May) 1927. These authors, working on passive transfer of local hypersensitiveness, recently reported a wheal similar to type 2. It was also induced on passively sensitized sites, but in their case it was induced by the intradermal injection of the offending pollen on some other part of the body. Their wheal, therefore, was also produced through internal channels. This emphasizes the importance of the constitutional route as a factor in the production of type 2 wheals.

but, like type 2 wheals, assumed their characteristic outline from the start, and retained this shape throughout.

In comparing these experimental wheals with clinical urticaria, another point is worthy of mention. It is a common observation that certain hypersensitive urticarias, the etiology of which is definitely known to depend on the ingestion of a certain food, will persist for a long time or recur at intervals, in spite of the fact that the offending substance has not been taken subsequent to the initial attack. That external irritations will prolong such an urticaria has been long recognized. As far back as 1888, Jacquet [18] demonstrated that, when the leg of a patient with a generalized urticaria was hermetically protected, the wheals and the pruritus were arrested on that part, while the rest of the body remained unaffected.

The experiments described by us apparently confirm the possibility of external traumas reviving or prolonging wheal reactions. The cells at the sites of injection, severely traumatized as a result of the immunologic wheal, apparently became similarly responsive to other forms of stimulation. Subsequent reactions could be elicited at some of the sites of previous wheals solely by various forms of external irritations, such as rubbing or scratching, etc. It is only a step further to conceive of the possibility of irritations arising from within, which would act similarly on these irritated or traumatized cells, and reproduce or prolong the original urticaria. What forms these irritating internal stimuli may assume is still a matter of conjecture. We have not yet succeeded in reviving a site of a previous wheal by nonspecific means through internal channels.

This communication is primarily an attempt to describe a form of constitutional urticaria in all its variations, as it was experimentally produced on the normal skin. Attempts have not been made to explain physiologically the mechanism of these reactions. This aspect of the subject is reserved for a future communication, when further studies will have been completed.

SUMMARY

1. The complete wheal reaction and its components, pruritus, erythema and wheal, as produced with our special technic, has been described in detail. Two types of erythema and two types of wheals, with their minor variations, have been portrayed, and cases demonstrating each, presented.

2. It has been shown that, as a result of this method of the production of wheals through internal channels, a hitherto undescribed wheal,

18. Jacquet, L.: Not sur le mode de production des elevures de l'urticaire, Ann. de dermat. et syph. **9**:529, 1888.

type 2, has been produced. This wheal developed outside, and never included, the site of injection.

3. The factors which influenced the reaction have been shown to fall under three main heads: (1) factors affecting local sensitization of the site; (2) those influencing the absorption of the offending protein, and (3) those concerned with the variations in technic. Each one of these has been presented in detail.

4. The similarity of these wheal reactions to those of certain forms of constitutional urticaria have been discussed from the point of view of morphology and symptomatology. The clinical course of both, so far as prolongation or revival of the reactions are concerned, have also been shown to be alike in certain respects.

CONCURRENT HERPES ZOSTER AND VARICELLA*

J. B. SHELMIRE, M.D.
AND
BEDFORD SHELMIRE, M.D.
DALLAS, TEXAS

Literature of the past few years dealing with the association of herpes zoster and varicella is so voluminous that a complete review of this subject will not be attempted. In 1915, Le Feuvre [1] placed the number of cases of associated zoster and varicella at forty. According to Low,[2] a total of fifty such cases had been recorded four years later. In an article published in 1924, Bokay [3] of Budapest, who was the first to report the possibility of a relationship between zoster and varicella (1888), found 200 cases recorded in fifty articles. It is estimated that during the past two years fully fifty examples of the association of these two diseases have been added to Bokay's list.

Reviewing the subject, the classification suggested by McEwen [4] in his excellent article dealing with this condition is repeated here. According to him, cases of zoster-varicella disease fall into four groups, namely:

(1) Herpes zoster in one patient followed by varicella in others who were exposed.

(2) Herpes zoster followed by varicella in the same patient but not followed by varicella in others who were exposed.

(3) Herpes zoster followed by varicella in the same patient, also followed by varicella in others who were exposed.

(4) Varicella in one patient followed by herpes zoster in others who were exposed.

According to McEwen [4] (1920), fully two thirds of the cases of zoster varicella belong to group 1. It has been estimated by us that, in view of later writings, fully 80 per cent of the cases reported belong to group 1. Next in frequency are the cases of so-called generalized

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* From the Department of Dermatology and Syphilology, Baylor University Medical School.

* Read at the Fiftieth Annual Meeting of the American Dermatological Association, May 12-14, 1927.

1. Le Feuvre, quoted by McEwen: The Association of Herpes Zoster and Varicella, Arch. Dermat. & Syph. **2**:205 (Aug.) 1920.

2. Low, quoted by McEwen: Arch. Dermat. & Syph. **2**:205 (Aug.) 1920.

3. Bokay, quoted by Roxburgh: Brit. J. Dermat. **39**:13 (Jan.) 1927.

4. McEwen, E. L.: Arch. Dermat. & Syph. **2**:205 (Aug.) 1920.

herpes zoster (herpes zoster generalisatus) or herpes zoster with aberrant vesicles. Cases of this type automatically fall into group 2 of McEwen's classification. In 1923, Parounagian and Goodman [5] gave a complete review of this phase of zoster-varicella disease and added one case to the already growing list.

Examples belonging to group 4 are rare. According to McEwen,[4] only four instances of varicella followed by zoster in contact patients, had been recorded as late as 1920. Roxburgh [6] cites Heard as having recorded additional cases of this type.

Cases falling into group 3 are by far the rarest of zoster-varicella disease. In 1920, McEwen [4] recorded the first authentic example of this type. "By liberal interpretation" he included two previously reported cases in this group. Five additional cases have come to our notice.

Morley [7] recorded the history of a boy, aged 5, who developed a right lumbar herpes zoster sixteen weeks after the onset of an anterior poliomyelitis The zoster eruption was followed in five days by a generalized varicellous eruption. Thirteen days later, two cases of varicella occurred in contact patients in the same ward.

Guszman [8] saw a man with clinically typical herpes zoster develop a generalized varicella-like eruption. Fourteen days later, the patient's son, with whom the father had been in contact, presented a typical chickenpox.

Vaglio [9] reported the case of a boy, aged 1 year, who developed a generalized varicellous eruption following a lumbar zoster. The patient's sister developed chickenpox twelve days later. Roxburgh and Martin [10] saw a man, aged 41, with a herpes zoster involving the areas supplied by the left second and third cervical nerves, develop a scanty eruption of vesicles on the trunk and limbs. A girl who had come in contact with this patient during the zoster stage developed a typical varicella with lesions on the scalp and palate.

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5. Parounagian, M. B., and Goodman, H.: Herpes Zoster Generalisatus, Arch. Dermat. & Syph. **7**:439 (April) 1923.

6. Roxburgh, A. C.: The Pathological Relationships of the Herpetic Diseases from the Clinical Standpoint, Brit. J. Dermat. **39**:13 (Jan.) 1927.

7. Morley, H. S.: Anterior Poliomyelitis, Herpes Zoster and Varicella in Sequence, Brit. M. J. **1**:552 (March 21) 1925.

8. Guszman, J.: A Contribution Concerning the Association Between Herpes Zoster and Varicella, Dermat. Wchnschr., no. 27, p. 779; Brit. J. Dermat. **36**:497 (Nov.) 1924.

9. Vaglio, R.: Pediatria, Naples **32**:172 (Feb. 1) 1924; International Survey of Pediatrics **7**:253 (April) 1924.

10. Roxburgh, A. C., and Martin, P. H.: Concurrent Herpes Zoster and Varicella, Brit. J. Dermat. **38**:286 (July) 1926.

REPORT OF CASES

CASE 1.—*History.*—P. S., a white man, aged 52, engaged in manual labor as cemetery sexton, gave a past history that was essentially negative. This patient was certain that he had not had chickenpox. Enlarged axillary and inguinal lymph glands had been present since boyhood. For three months prior to his first visit to the clinic, he had suffered intense neuralgic pains of the right side of his face and head. On Oct. 29, 1926, he consulted the dental department of the Baylor Hospital because of "blisters on the tongue" and pain in the right lower gum. At that time, groups of vesicles were noted on the dorsal surface of the anterior two thirds of the right half of the tongue, and one vesicle on the right lower gum below the canine. Two days later, a vesicular eruption appeared over the entire anterior two thirds of the right half of the tongue, dorsal and ventral surfaces, the right lower gum, and the buccal mucous membrane. Owing to the coalescence of vesicles and their alteration by moisture, a grayish membrane or slough was present in some areas. At this time, a few vesicular lesions were irregularly scattered over the right side of the face and scalp. This corresponded to the area over which the patient had suffered neuralgic pains for three months previously. A diagnosis of herpes zoster was made at this time, and he was admitted to the hospital. Within twenty-four hours, the zoster eruption was at its maximum, characterized by vesicles varying in size from that of a pinhead to that of a pea, roughly following the distribution of the mandibular division of the right trigeminal nerve, namely: the internal and external skin surfaces of the right ear; the central portions of the right half of the scalp, the right cheek, the right half of the chin and lips, the right half of the anterior two thirds of the tongue and the buccal surface of the right cheek. The line of demarcation on the tongue and chin was remarkably distinct. As there was a motor paralysis of the right side of the face and vesicular lesions within the external auditory meatus of the right side, it was decided that the seventh geniculate ganglion might also be the seat of zoster disease. Many of the vesicular lesions then became hemorrhagic and gangrenous, showing every symptom of herpes zoster hemorrhagicus and gangrenosus.

On November 7, four days after admission to the hospital, pea-sized macules and vesicles appeared over the trunk and extremities. The macules were erythematous. The vesicles arose from a clear base or were surrounded by a pink erythematous halo; the surface was smooth or there was umbilication in the center. Some vesicular lesions became hemorrhagic or gangrenous; others followed the course of a typical benign chickenpox. New lesions continued to form until death. At this time, the entire cutaneous surface was studded with a varicella-like eruption. Isolated vesicular lesions were present on the hard and soft palates and the remains of one vesicular lesion was found at autopsy on the posterior wall of the larynx. Crusted lesions were scattered over the scalp.

On admission, the temperature was 100 F. With the advent of the generalized vesicular eruption, it rose to 102 F., and for twenty-four hours previous to death it averaged 104.6 F. Because of the marked swelling of the tongue and buccal mucous membrane, respiration became increasingly difficult, which made it necessary to insert a tracheotomy tube thirty-six hours before death. About twenty-four hours before death, areas of consolidation were evidenced at the bases of both lungs.

Laboratory Examinations.—The total number of red blood cells ranged from 3,840,000 to 4,400,000 per cubic millimeter. On admission, the total number of

white blood cells per cubic millimeter was 8,300, of which 65 per cent were polymorphonuclears. Twenty-four hours after the advent of the generalized eruption, the total number of white blood cells increased to 16,900 per cubic millimeter, with 81 per cent polymorphonuclears. At the time of death, the total number of white blood cells was 22,000, with 82 per cent polymorphonuclear leukocytes. The results of the urinalysis, Wassermann and Kahn tests were negative. The blood culture was negative on two occasions. The only abnormality of the blood chemistry was the evidence of a marked nitrogenous

Fig. 1 (case 1).—Zoster eruption of right half of tongue and right side of face with vesicles of the generalized eruption on the forehead.

retention; urea, 60; urea nitrogen, 28; and nonprotein nitrogen 58 mg. per hundred cubic centimeters of blood. The spinal fluid (obtained at autopsy) showed 406 white blood cells per cubic millimeter, predominantly polymorphonuclear leukocytes. Attempts to reproduce the disease by the inoculation of the vesicular fluid into scarified corneas of rabbits proved futile.

Necropsy Report.—Necropsy was performed by Dr. O. T. Woods. The body was that of a white man, apparently about 45 years of age. Body heat was

present and rigor mortis was absent. Scattered over all the skin surfaces were many blood-crusted lesions averaging about 5 mm. in diameter. Practically all of these were not raised above the surface of the skin. There was an equal number of pinkish superficial vesicles averaging about 5 mm. in diameter. These were filled with a clear fluid. On the removal of the covering, the bases were seen to be hemorrhagic, which accounted for the pinkish appearance of the vesicles. On the right side of the face, covering the area of distribution of the mandibular division of the fifth nerve, there were partially necrotic black crusted lesions averaging about 4 mm. in thickness.

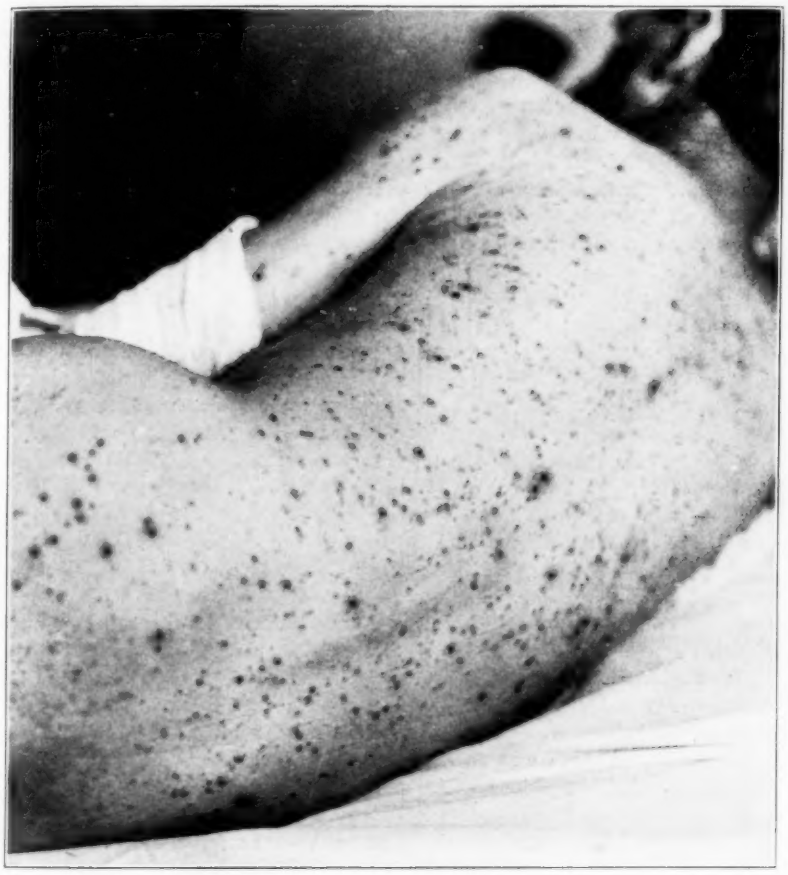

Fig. 2 (case 1).—Generalized varicella-like eruption following herpes zoster.

A rubber tube 0.9 cm. in diameter projected through an unsutured tracheotomy incision measuring 3 cm. in length. The surfaces of the wound were covered with a grayish-brown exudate. The mucous membranes on the right half of the mouth and the right half of the anterior portion of the tongue, were covered with a grayish-black necrotic membrane about 4 mm. in thickness. There was not any edema of the subcutaneous tissues. There was a marked enlargement of the axillary lymph nodes. Some of the larger lymph nodes measured 3 cm. in diameter; they were soft, discrete and freely movable. The

cervical, epitrochlear, postauricular and occipital nodes were similarly enlarged and had an average diameter of about 1.5 cm. The pupils were regular; the right about 9 mm. in diameter, and the left about 6 mm. The tissues in the anterior portion of the neck were swollen, edematous and hyperemic; on palpation crepitation occurred in the posterior inferior triangle and in the areas in front of the sternomastoid muscles. Other noteworthy external changes were not seen.

The fat in the midline incision was about 0.7 cm. thick and pale orange-yellow. The peritoneal cavity was free from fluid, and the peritoneal surfaces were smooth and glistening. The entire colon was moderately distended with gas. The appendix was found retrocecally, and was bound down by firm fibrous adhesions. The spleen was adherent to the lateral wall of the body by easily torn fibrous adhesions. The transverse colon was adherent to the under surface of the right lobe of the liver by easily torn fibrous adhesions.

The posterior portion of the upper lobe of the left lung was adherent to the wall of the chest by easily torn fibrous adhesions. The pleural cavity was free from fluid, and the remaining pleural surfaces were smooth and glistening. The posterior five sixths of the lower lobe was almost completely consolidated, and, on section, a yellowish exudate could be squeezed from the smaller bronchioles. The tissues in an area approximately 0.5 cm. in diameter which surrounded the bronchioles were firm and more grayish than the intervening areas. The tissues in the posterior portion of the upper lobe were similarily involved, but in addition contained several softened necrotic areas about 1 cm. in diameter. These areas contained a grayish-brown exudate surrounded by a brownish-black membranous-like layer. The anterior portions contained only a few scattered grayish nodular areas about 0.5 cm. in diameter. The intervening lung tissue was of a relatively normal gross appearance. The posterior portions of the right lung including most of the lower lobe, were almost completely consolidated and contained many brownish-black necrotic areas about 1 cm. in diameter. The anterior portions of this lung were like those of the left lung. The pulmonary artery and its main branches were free from blood clots. The mucosa of the trachea was hyperemic and edematous and contained a moderate number of scattered grayish-yellow membranous-like plaques which varied from 2 to 6 mm. in diameter. The tissues surrounding the larynx and the upper portion of the trachea were edematous and moderately hyperemic, and were easily separated by finger dissection. The tissues of the trachea surrounding the rubber tube were necrotic in a narrow margin. In the posterior notch of the larynx there was an area about 1.5 by 0.5 cm. which was covered with a grayish exudate. The remaining part of the mucosa of the larynx was smooth.

The pericardial sac contained about 12 cc. of a clear yellowish fluid. The pericardial surfaces were smooth and glistening. The heart was only slightly larger than the owner's clasped fist. Noteworthy changes were not seen in the pulmonic or tricuspid valves. There was a slight fibrous thickening of the margins of the cusps of the aortic valve. The beginning of the aorta was smooth and elastic. Noteworthy changes were not seen in the mitral valve. On section, the myocardium was more grayish than normal, and its surfaces appeared moist.

The capsule of the liver was adherent to the diaphragm by easily torn fibrous adhesions, which on removal left about half of the surface of the liver denuded. The liver was about normal size, and firm in consistency. On section, the cut margins and the sectioned surfaces were more grayish-brown than

normal, and the center of the lobules of the liver was indistinct. The gallbladder was about normal size, and the bile could readily be expressed into the duodenum. The pancreas was flabby and the lobulations were distinct.

The spleen was firm and moderately enlarged, measuring 15 by 9 by 6 cm. The capsule was uniformly thickened to about 1 mm. On section, the increase in connective tissue in the pulp gave it a lacy appearance. The pulp scraped poorly from the cut surfaces, and the cut margins bulged on approximation.

The left kidney was about normal size, and contained at least four subcapsular, retention cysts averaging about 0.7 cm. in diameter. The capsule stripped with slightly increased resistance, which left a slightly granular surface. On section, the tissues were grayish, and the cortical markings were indistinct. The conditions found in the right kidney were the same as those in the left. The cut surfaces appeared distinctly moist and waxy. There were not any noteworthy changes in the suprarenal glands or in the upper portions of the ureters.

The mesenteric lymph nodes, retroperitoneal lymph nodes and mediastinal lymph nodes were enlarged everywhere and averaged about 2 cm. in diameter. On section, they were pale and a few from the mediastinum contained areas of anthracosis.

The urinary bladder contained about 100 cc. of slightly cloudy urine. The mucous membrane was smooth and glistening. Noteworthy changes were not seen in the small and large bowel, as viewed from the outside.

The stomach contained about 100 cc. of brownish-black fluid. The mucosa appeared coarsely granular, but was intact everywhere.

There were no noteworthy changes in the inner table of the skull or in the dura. There was a slight grayish thickening in the leptomeninges around the blood vessels. The fluid in the leptomeninges appeared slightly cloudy. Noteworthy changes had not occurred in the multiple sections of the cerebral hemispheres, cerebellum, brain stem, pons or medulla. The left gasserian ganglion appeared normal grossly. The right gasserian ganglion contained an area of hemorrhage replacing about one third of the tissues.

Microscopic Examination of Skin.—The surface of epithelium was missing in localized areas. The underlying tissues were hemorrhagic and were invaded in the surface layers by packed leukocytes which formed a circumscribing band. There were many bacterial masses in the exudate on the surface. A few scattered lymphoid cells extended along the blood vessels of the skin and subcutaneous tissue. The necrosis was more extensive and was gangrenous in a few of the surface areas. One of these gangrenous areas involved the muscle tissues of the tongue.

Approximately half of the gasserian ganglion was hemorrhagic, and the nerve tissues were partially necrotic. Lymphoid cells in moderate numbers invaded the fibrous septums between the nerve bundles. A few of the outlying hemorrhagic areas within the nerve bundles contained a moderate number of lymphoid cells and leukocytes.

The lungs showed suppurative and gangrenous pneumonia of a peribronchial type. Bacterial masses were abundant in many of the pneumococcic foci. There was inflammatory edema of the intervening areas of the lung, and marked hyperplasia of the lymph nodes. The lymph follicles were completely erased and the lymphoid cells were mostly of the large type. The kidneys showed marked parenchymatous changes in the tubular epithelium. Noteworthy changes were not observed in the suprarenal glands nor in the pancreas.

The intestine showed marked hyperplasia of the lymphoid tissues of the wall of the bowel. There were mucin-like bodies in the cerebral cortex bordering the leptomeninges, and moderate hyperemia of the brain tissue.

CASE 2.—L. S., white, aged 27, daughter of the patient whose case was reported in case 1, fourteen days after the development of herpes zoster in her father experienced a general malaise for a period of two days. The temperature ranged from 100 to 101 F. On the third day, a dozen pea-sized macular lesions and two pinhead-sized, barely palpable papules with their surfaces capped with tiny vesicles appeared on the upper portion of the back. The diagnosis was doubtful until the patient returned to the clinic two days later. At this time, pea-sized vesicles were scattered over the trunk, face and upper extremities. Vesicles arose from normal skin or were surrounded by a pink areola. The fever had entirely disappeared at this time. A diagnosis of varicella was made. Twenty-four hours later, most of the vesicles were replaced by thin crusts. Several additional vesicles showed umbilication in the central portions. There were one vesicle on the soft palate and two crusted lesions on the scalp.

This patient had never had herpes zoster or chickenpox. She had not come in contact with children recently, nor had she been exposed to varicella.

RECENT RESEARCH ON HERPETIC DISEASE

Because of recent investigation, a close relationship is considered to exist between herpes simplex, herpes zoster and varicella. Some observers claim that herpes zoster is due to a modified herpes simplex virus; others claim that the etiologic agents of herpes zoster and varicella are identical or closely related. The acidophilic intranuclear inclusion bodies first described by Tyzzer [11] in varicella and later by Lipschütz [12] in herpes simplex and herpes zoster are common to all three conditions. These bodies are considered by Lipschütz [12] to be characteristic of the diseases of the filtrable virus group. While the etiology of herpes simplex seems to be an estabiished one, the true nature of herpes zoster and varicella is still a much mooted question.

It has been shown that if the vesicle contents from a patient suffering from herpes simplex (herpes facialis, herpes labialis, herpes genitalis) are rubbed into the scarified cornea of a rabbit, a vesicular eruption followed by an intense keratoconjunctivitis is produced with great regularity. By direct inoculation into the brain of these animals, encephalitis with a characteristic clinical picture and a fairly definite period of incubation can be produced. This keratitis or encephalitis is in turn transmissible from rabbit to rabbit indefinitely or in series. This transmission in series is looked on as proof that the vesicle contents in herpes simplex contain a living agent or virus. When a keratitis on a scarified cornea of a rabbit is produced by a virulent strain of the herpes simplex virus,

11. Tyzzer, cited by Cole and Kuttner: J. Exper. Med. **42**:799 (Dec. 1) 1925.

12. Lipschütz, B.: Arch. f. Dermat. u. Syph. **136**:428, 1921; cited by Cole and Kuttner: J. Exper. Med. **42**:799 (Dec. 1) 1925.

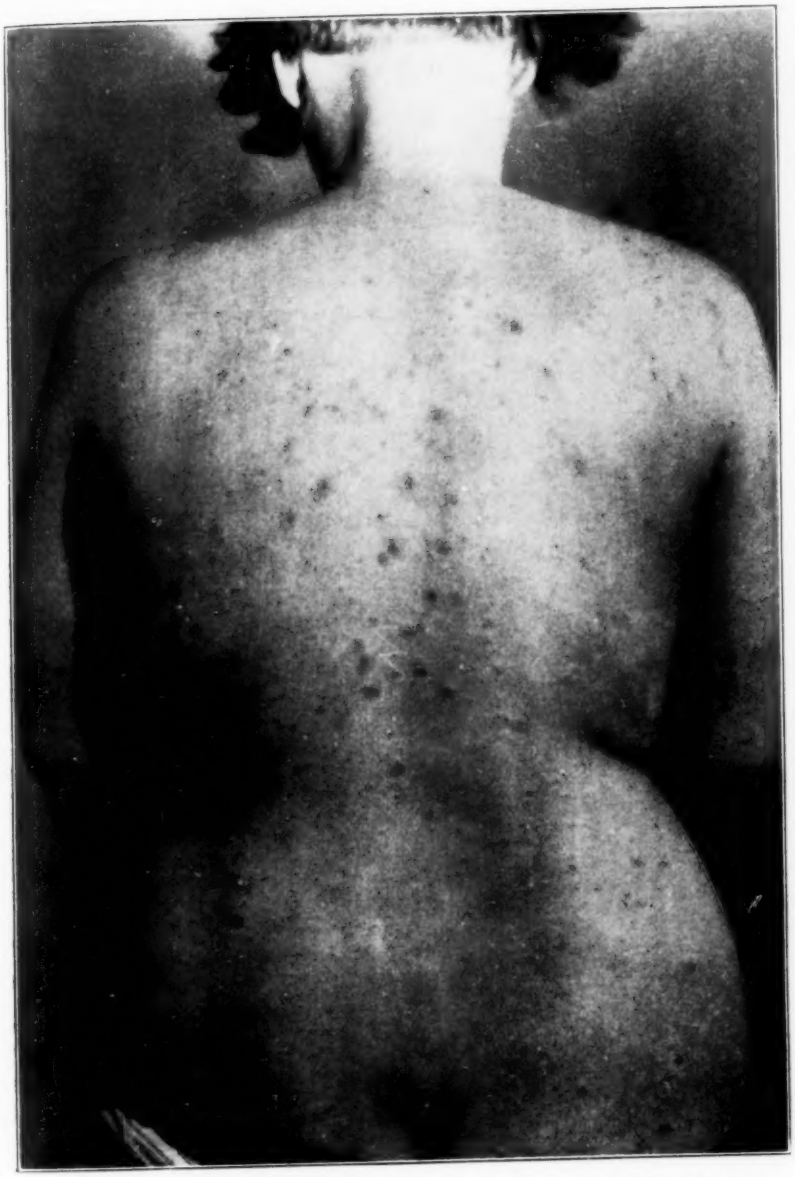

Fig. 3 (case 2).—Generalized varicella-like eruption in daughter.

the virus usually spreads to the brains of these animals, causing a herpetic encephalitis. According to Perdrau,[13] whose paper is freely quoted here, the virus will travel to the central nervous system and produce a fatal encephalitis if it is inoculated by certain other routes, as into the skin by deep scarification, into the testicle, into the sheath of a peripheral nerve or into certain mucous surfaces. Animals that have recovered from a herpetic keratitis or encephalitis are usually found to be able to resist the intracerebral inoculation of hundreds or thousands of lethal doses of the virus, showing that they are endowed with a certain immunity from the previous inoculation.

On the skin of a rabbit, according to most observers, neither the passage virus nor the contents of herpetic vesicles from man give more than slight erythema and edema of the inoculated area. Gildemeister and Herzberg,[14] Maitland [15] and Bedson [16] were able to cause a vesicular eruption on the soles of guinea-pigs by inoculating the plantar epidermis with the virus of herpes. According to their reports, the plantar eruption in these animals was similar to, but not identical with, the herpes simplex lesion in man.

While most observers have agreed that the virus of herpes progenitalis and that of herpes simplex are identical, Lipschütz [17] contended that the two work differently on rabbit corneas, that there is a difference in the incubation periods and that there are clinical and histologic differences between the evoked eruptions. He claims that the nuclear inclusion bodies of the two are different and that there is an absence of cross-immunity between herpes febrilis and herpes genitalis on the corneas of rabbits and, lastly, that the virus of herpes genitalis will not infect the corneas of guinea-pigs. Other workers do not give credence to his observations.

We have not carried out any research work with the virus of herpes simplex; yet extensive experimentation with this virus carried out at the clinic of Professor Pautrier in Strassbourg was viewed by one of us. Summarizing the work on herpes simplex, it can be said that a virus, highly infectious for rabbits, has been isolated from these cases; yet the clinical picture produced by transference of the virus to animals is not identical with herpes simplex in man.

Although a great amount of experimental work has been done during recent years on herpes zoster, most of it has been contradictory, and

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13. Perdrau, J. R.: Herpetic Diseases, Brit. J. Dermat. **39**:1 (Jan.) 1927.

14. Gildemeister, E., and Herzberg, K.: Deutsche med Wchnschr. **51**:97 (Jan.) 1925.

15. Maitland, quoted by Bedson: Brit. J. Dermat. **39**:26 (Jan.) 1927.

16. Bedson, S. P.: Brit. J. Dermat. **39**:26 (Jan.) 1927.

17. Lipschütz, B.: Arch. f. Dermat. u. Syph. **149**:379, 1925, and cited after Roxburgh (footnote 6).

little has actually been added to our knowledge of this disease since 1900, when Head and Campbell [18] first described the lesions present in the posterior root ganglions and the adjoining segments of the spinal cord in herpes zoster. Recent work by Kundratitz,[19] when verified, may materially add to the knowledge concerning this condition.

Although isolated positive results have been obtained, it is generally agreed that the vesicle contents in herpes zoster are avirulent for rabbits. Inoculation of a scarified cornea of a rabbit in the case reported here gave negative results.

In 1921, Lipschütz [12] reported the successful inoculation of rabbits with material from herpes zoster. About seven cases with clinically typical herpes zoster were studied. Vesicular fluid obtained early in these cases and rubbed into the scarified cornea of a rabbit was said to have given positive results in four instances. This observer claims that his positive observations have been confirmed by Marineso and Draganesco, Truffi, Mariani and others. According to Cole and Kuttner,[20] two of the writers quoted by Lipschütz as having confirmed his experiments with positive inoculations, regard their own work as inconclusive, while about a dozen other observers report negative results following the inoculation of herpes zoster material into the scarified corneas of rabbits. Cole and Kuttner,[20] after painstaking and laborious experiments, reported negative results. These observers were careful to select cases of idiopathic herpes zoster and to exclude cases of so-called zosteriform herpes and symptomatic herpes zoster. In making inoculations into rabbit corneas, the technic recommended by Lipschütz was followed. The material obtained was selected from fresh vesicles of seven cases of zoster and the material injected into about thirty rabbits, monkeys (macacus and vervets) and guinea-pigs. Corneal, intracerebral, intraspinal, intracutaneous and intratesticular inoculations were employed. Their observations seem conclusive. They were not able, in a single instance, to confirm the observations of Lipschütz and successfully inoculate animals with material obtained from fresh vesicles of clinically typical herpes zoster.

Experiments by Kundratitz [19] seem to indicate that the virus of varicella and that of herpes zoster are either identical or closely related. This observer found that the fluid from the vesicles of a typical zoster eruption, when inoculated into the skin of young children, produced a varicellous eruption. In two instances, he was able to pass the condition from child to child. The intracutaneous inoculation of twenty-eight

18. Head and Campbell: Brain **23**:353, 1900.

19. Kundratitz, K.: Ztschr. f. Kinderh. **39**:379, 1925.

20. Cole, R., and Kuttner, A. G.: The Problem of the Etiology of Herpes Zoster, J. Exper. Med. **42**:799 (Dec. 1) 1925.

children who had previously had neither chickenpox nor zoster, gave seventeen positive and eleven negative results. A patch of clear vesicles on an erythematous base, developing from nine to twelve days after inoculation, was considered as a "take." Two of the children inoculated with zoster material developed typical varicella with lesions on the face and scalp. Several cases of varicella could be traced to contact with children who had developed localized positive reactions from inoculation with zoster material. Lipschütz [17] found in several of these provoked varicella-like eruptions nuclear inclusions described by him as characteristic of virus disease. Children who had previously had chickenpox were immune to the inoculation of zoster material, while those who recovered from the induced varicella-like eruptions from inoculation with zoster material were later found to be immune to chickenpox. Positive reactions were obtained only in children under 5 years of age. So far as we have been able to ascertain, the experiments of Kundratitz have not been confirmed by other observers. Should further experimental work confirm his observations, there will be little doubt as to the identity of the viruses of the two diseases.

By cross complement-fixation tests, Netter and Urbain [21] seem to have established the close relationship of herpes zoster and varicella. Their conclusions were based on the serum of 100 persons affected with herpes zoster and 24 persons suffering from chickenpox. A positive complement-fixation test was found in 93 per cent of the cases of herpes zoster and 91.7 per cent of cases of varicella. These observers used as antigens contents or crusts of herpes zoster vesicles and found positive complement-fixation tests when the blood serum of patients convalescent from varicella was used. In a like manner, positive fixation tests were obtained when contents of varicella vesicles were tested with serums of patients suffering from herpes zoster. These results have been criticized by Roxburgh and others. Lauda and Silberstern [22] were not able to confirm the positive cross complement-fixation tests, although they followed the technic described by Netter and Urbain. In most of the experiments, the antigen used was furnished by French observers. Two serums sent for examination from Vienna to Netter and Urbain likewise proved to be negative.

Although attempts to transmit varicella to animals have met with universally negative results, Kling [23] has successfully vaccinated children against chickenpox by inoculation with fresh vesicular fluid from active

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21. Netter, A., and Urbain, A.: The Relation Between Herpes Zoster and Varicella, Compt. rend. Soc. de biol. **94**:98 (Jan.) 1926.

22. Lauda, Ernst, and Silberstern, Ernst: Question of Serologic Relations Between Zoster and Varicella, Klin. Wchnschr. **4**:1871 (Sept. 24) 1925.

23. Kling, cited after Cole and Kuttner (footnote 20).

cases of this disease. Contradictory results have been reported by other observers. Some experimenters have reported the development of a vesicle or papule at the site of inoculation or a generalized varicella-like eruption; others have reported that an obvious lesion did not occur after inoculation with varicella material.

SUMMARY

During the course of herpes zoster of the right fifth nerve distribution, a patient developed a generalized, extensive vesicular exanthem closely resembling varicella. Singularities of the zoster eruption in this case were the involvement of the right half of the tongue and buccal mucous membrane of the right cheek and motor paralysis of the right half of the face, infranuclear in type. The generalized eruption following the zoster was extensive, involving the glabrous skin of almost the entire body, the oral mucous membrane not already the seat of zoster lesions and the scalp. Necropsy revealed pathologic changes in the right gasserian ganglion similar to those found in the spinal root ganglion in herpes zoster of dorsal root distribution. The disease could not be transmitted to rabbits by the inoculation of vesicular fluid into their scarified corneas. Fourteen days after the appearance of the zoster in the father, a daughter who had not been exposed to chickenpox developed a clinically typical varicella eruption with lesions of the scalp and mouth.

Medical Arts Building.

DISCUSSION

DR. SCHAMBERG, Philadelphia: The subject Dr. Shelmire has presented is of great interest. When an alleged relationship of varicella to herpes zoster was brought up, I was somewhat skeptical regarding the relation of the two diseases which were so unlike—one a common, highly contagious disease among children and the other a much less common disease, occurring chiefly among adults. I have kept in touch with the literature on the subject, and I am forced to admit that it deserves serious consideration. I think the clinical evidence is less convincing than some of the laboratory evidence. I am sure that if some one would suggest that exposure to measles was likely to induce herpes zoster later, one could in a few years cite many cases in which one condition developed after the other. The channels of infection of the exanthemas are devious and mysterious, and not too much credence can be placed in the statement that a patient has not been exposed to varicella. The work of Netter on cross complement-fixation has impressed me. If it is confirmed that the blood from patients with varicella and those with herpes zoster cross-fix the complement of each other, then strong evidence of a true relationship between these diseases is added.

In connection with cases of generalized zoster, it appears to me that the virus instead of being limited to an attack on one ganglion in the spinal cord attacks one or more isolated cells in other ganglions. In zoster of the body, one is dealing with a posterior poliomyelitis. I think that we dermatologists can contribute to the problem under discussion by taking careful histories in all cases of herpes zoster. We should find out whether these patients have had varicella in childhood. One attack of varicella almost invariably confers immunity. I have never seen a second attack of varicella. I have seen many attacks in adults. This occurs rarely in Europe, but much more frequently in the United

States because of our more scattered rural population. I do not understand why a child who has had varicella in childhood should develop herpes zoster at a later period if there is an actual etiologic relationship. Concerning this point histories would be useful. The whole subject is extremely interesting, and one cannot afford to be dogmatic; one should retain an open mind.

Dr. McEwen, Chicago: I think Dr. Shelmire is to be congratulated on his paper. In these cases it is of vital importance that the patient should never have been exposed to varicella before. The question of the aberrant vesicle in herpes zoster has always been of interest to me. In the cases at the clinic we have made a routine examination of the entire skin, looking for these scattered vesicles, and while the cases have not been numerous, I have been surprised at the number of times that we have been able to find vesicles at other points. In view of this association of zoster and chickenpox, I think it is extremely important that every case of zoster be examined for the aberrant vesicle.

Dr. Shelmire: I wish to stress what has been said about obtaining a detailed history in all of these cases. In every case of zoster and varicella, a careful inquiry should be made as to exposure, and a record should be kept. If the clinicians will do this, with the help of the pathologists and bacteriologists, the questions concerning this eruption may be settled to the satisfaction of all.

Miscellany

ALOPECIA AREATA AND EMOTIONAL STRESS

WILLIAM ALLEN PUSEY, M.D.
CHICAGO

I have been consulted by a young man with alopecia areata who gave the most direct history of association of alopecia areata and emotional stress I have ever encountered. The patient was, apparently, a well balanced young man, a railroad baggageman. About eight weeks ago he was on a fast mail train between Chicago and Milwaukee which struck a bus loaded with young school children and killed between thirty-five and forty of them. This man was standing in the baggage car, saw the bus coming down hill to a crossing that the train going seventy miles an hour was to pass and saw the bus go on to the track, and the train pick it up and carry it a quarter of a mile until it could stop. His expression was that to see the thing happen and then to go and see forty or fifty dead children in a pile was too much for him. He did not give evidence of exaggerating his shock, but the shock unnerved him so completely that he had not, until the day he consulted me, gone back to his occupation. About ten days to two weeks after the experience he discovered his hair coming out in patches and when I saw him he had several large patches of alopecia areata. He had never had alopecia areata before.

The case is recited, not as proving anything, but as showing at least in this case, apparently, a definite relationship between mental shock and alopecia areata.

Correspondence

SOCIETY REPORTS

The following letter on society reports comes from Dr. Oscar Sprinz, editor of the *Zentralblatt für Haut-und Geschlechts-krankheiten,* in response to an editorial in the ARCHIVES on the same subject. It touches on weaknesses in society reports that we have particularly referred to in these columns, and it is earnestly commended to the attention of secretaries and other reporters of clinical societies, and to those who present cases at the meetings.

To the Editor.—As editor of the *Zentralblatt für Haut-und Geschlechts-krankheiten* I was very much interested in your article in the ARCHIVES OF DERMATOLOGY AND SYPHILOGY, vol. 17, no. 1, p. 105. I am taking the liberty of sending you some additional remarks, hoping you will be kind enough to publish them in one of your issues.

The *Zentralblatt für Haut-und Geschlechts-krankheiten* is, as far as I know, the only journal which reports the transactions of the different American societies of dermatology. I have always maintained the opinion that it is well worth while to publish all the demonstrations in our *Zentralblatt,* for the opinions of prominent American dermatologists and the discussions of doubtful cases often throw a light on difficult problems and give useful therapeutic hints. Your frankness in criticizing publicly your own transactions encourages me to add several words to attract attention to some defects, hoping in this way to remove them.

1. Why do you present so many doubtful cases as "a case for diagnosis"? If those who present the case and discuss it are not quite sure how to diagnose syphilis, tuberculosis or psoriasis, the reader, not seeing the patient, will surely not know what is the matter. The cases ought to be observed sufficiently in the clinic and in the laboratory to make a diagnosis possible. But I am convinced that sometimes the cases are presented only because on that very day the eruption is especially visible, even if there has not been sufficient time for thorough examination. There will always be such exceptions in dermatology, but the remark that "there has been no time for histologic examination" must not cover superficiality.

2. It is necessary to spell the Latin titles better; the terminations are often entirely wrong.

3. Often it is said that the case has been presented previously; but in following the references of the transactions one is disappointed not to find the case, because it has not been presented, the references are incorrect, or it was presented by some one else and cannot be identified under the same name. It is to one's own interest to be more correct in this line, and our *Zentralblatt* would profit by it, because we are used to making exact references to previous presentations.

4. Finally, we often find the remark that after the examination is finished the results will be published. For months we retain the report, always hoping for the following publication, but in vain. Thus we are not able to bring the case under the right group of diseases in our *Zentralblatt,* and, therefore, it will easily be overlooked by the reader.

I should be very much obliged, if you would kindly examine my proposals —they partly correspond to yours— and I hope it will be possible to remedy the defects.

OSCAR SPRINZ, M.D., Berlin, Germany.

Tonics and Sedatives

ETIOLOGY OF BALDNESS

The following theory of the etiology of baldness is new, we believe, and should be added to the already innumerable explanations of that unhappy condition. If it involves some rather extreme wrenches in our knowledge of physiology and anatomy, it does not differ in these respects from many of the other theories, and it cannot be said to lack originality. The explanation is to the following effect:

The hair roots continually grow deeper in their search for nourishment, much as the roots of a tree will grow deeper and deeper to get water. These hair roots gradually grow down into the skull and, by middle life—sometimes earlier, sometimes later—penetrate the skull and finally reach the brain. When that situation occurs, one of two things happen: If the roots find gray matter, the hairs turn gray; if they do not, it falls out.

This concept, at least, can be offered as an offset to the intelligence theory of baldness.

Abstracts from Current Literature

A New Treatment for Vincent's Angina. R. G. Reeves, Arch. Otolaryng. **7**:166 (Feb.) 1928.

Excellent results are reported from the local application of acriviolet, a combination of acriflavine and gentian violet in 2 per cent solution.

Rattner, Chicago.

Treatment of Tabes Dorsalis by Epidural Injections of Neoarsphenamine: Preliminary Report. G. B. Hassin, J. A. M. A. **90**:605 (Feb. 25) 1928.

Hassin injects neoarsphenamine into the epidural space, using a spinal puncture needle inserted through the sacral hiatus into the sacral canal. Doses, the same as in intravenous therapy, are given twice weekly for about four weeks. So far, forty patients have been treated by this method. The most striking improvement was in the gait, the Romberg sign, the ataxia and the shooting pains. Indefinite and inconstant results were obtained in optic atrophies and crises. Of 125 injections given, only one proved disastrous. In that instance, death occurred with symptoms of myelomalacia. In two other cases, serious symptoms appeared.

Severe Granulocytic Aplasia of the Bone Marrow: Report of a Case Following Arsphenamine Treatment in Congenital Syphilis. K. Dodd and S. J. Wilkinson, J. A. M. A. **90**:663 (March 3) 1928.

The patient, aged 11, had latent congenital syphilis (four plus Wassermann reaction, but no clinical symptoms). She had received four injections of sulpharsphenamine when she complained of symptoms suggesting severe infection rather than arsenical poisoning. Blood counts showed marked and progressive leukopenia, with absence of polymorphonuclear leukocytes. A necropsy showed almost complete aplasia of the bone marrow. The authors found twenty previous reports of similar cases, but theirs is the first in a child. Therapy has not proved successful in these cases. Perhaps careful attention to the early signs of intolerance and recognition of the significance of the first changes in the blood, followed by injections of sodium thiosulphate, might prevent serious developments.

The Etiology and Results of Treatment in Angioneurotic Edema and Urticaria. F. R. Menagh, J. A. M. A. **90**:668 (March 3) 1928.

The author's series comprised 260 cases. By sensitization tests he was enabled to discover the cause of the condition in 30 per cent of the cases. In about 50 per cent, disease of the biliary tract was the etiologic factor; while in 10 per cent, these two causes were combined and in the remaining 10 per cent, the cause evaded search. The author employed transduodenal drainage to determine the status of the biliary tract, which in his series was the only part of the gastro-intestinal system that was related etiologically to the disease. Organisms cultured from the bile were allergically tested, and vaccines were employed therapeutically when the allergic tests were positive. Nonsurgical biliary drainage was used, with some measure of success in many of the cases. The author concludes by stressing the importance of disease of the biliary tract in the etiology of urticaria and angioneurotic edema.

Quantitative Study of Clinical Ultraviolet Sources. H. Goodman and W. T. Anderson, J. A. M. A. **90**:671 (March 3) 1928.

The authors discuss the confusion and inaccuracy that abounds in medical literature about the dosage of ultraviolet rays. To throw some light on this

subject, they have examined many sources of ultraviolet radiation (carbon and mercury arc sources) and present a table of their investigation. They suggest the designation of intravital, vital and extravital for the three zones of ultraviolet radiation that have medical interest. The first does not have a known biologic effect in vertebrates, the second and third have definite value in therapy and in human well-being.

HEREDITARY DYSTROPHY OF THE HAIR AND NAILS. A. W. JACOBSEN, J. A. M. A. **90**:686 (March 3) 1928.

The author describes a family group in which congenital alopecia and dystrophy of the nails were traced through five generations. Only four families with these hereditary abnormalities have been reported previously. The author saw two of this family group: a mother, aged 41, and her child, aged 7. Both had scanty, fine hair and ridged, friable nails. While the cause is unknown, dysthyroidism is suggested.

MICHAEL, Houston, Texas.

THROMBO-ANGITIS OBLITERANS. H. A. PEACOCK, Proc. Staff Meetings Mayo Clinic **3**:40, 1928.

A case was cited with involvement of both lower extremities and the left hand, with symptoms confined entirely to the left hand.

In the discussion, Dr. E. V. Allen cited 300 cases. He concludes that the use of tobacco is a definite etiologic factor; the disease is increasing in incidence with a considerable increase in the percentage of gentile people involved; gangrene is not inevitable, symptoms may go and minor trophic lesions may heal; intravenous typhoid vaccine is the best single means of relieving pain. All 300 cases occurred in men. Amputation of the fingers is sufficient for cases involving the upper extremities, but in the lower extremities amputation must be at the knees.

RATTNER, Chicago.

STREPTOCOCCAL PITYRIASIS. H. HAXTHAUSEN, Lancet **2**:370, 1927.

By his special method of cultivating streptococci from the skin, using 10 per cent blood agar with a 1:100,000 solution of crystal violet, which inhibits the staphylococcus and does not affect the streptococcus, Haxthausen is able to cultivate streptococci on solid mediums, whereby one can form a good idea from the quantity of colonies of the number of streptococci in the original material. By this method, he confirms the opinion of Sabouraud and Adamson and others that there are dry scaling rashes, occurring mostly on the face in children, which are due to the streptococcus and do not belong to seborrhoic eczema, as most authors thought. The lesions showing laminated streaky desquamation, have been called by Sabouraud "impetigo sicca," and by Adamson "chronic impetigo." The author proposes the name "Pityriasis streptogenes," because the disease is secondary to impetigo only in a small number of cases, while the majority—classed by most people as seborrhoic eczema—occur primarily as a pityriasis and preserve this appearance in their future course. Haxthausen found that they often start from the angles of the mouth and nostrils; that they are frequently hypersensitive to light; that they are often easily irritated by soap, cold cream, petrolatum and hydrous wool fat and others; that they occur not only on the face but also rarely on the scalp, and on the body with a predilection for the lateral parts. The disease occurs mostly in children from 6 to the age of 14, but also occurs frequently in adults, more often in women than men. As a treatment he suggests the application of zinc ointment with from 1 to 2 per cent coal tar.

EPIDERMAL STREPTOCOCCAL CONDITIONS STUDIED BY A NEW METHOD OF CULTURE. M. HAXTHAUSEN, Ann. de Dermat. et Syph. **8**:201, 1927.

By adding a certain concentration of crystal violet solution to culture mediums, which inhibits the growth of the luxuriant staphylococci colonies and permits the

streptococci to grow, the author has made the following observations in 600 cultures of healthy and diseased skin: in 92 cultures made from normal skin, only 7 showed streptococci. Diseased skin—impetigo and other diseases, known as of streptococcus etiology, not included—showed streptococci in 15 per cent of the cases. But those cultures made on solid mediums showed only isolated colonies of streptococci. In impetigo and ecthyma there were found almost always enormous numbers of streptococci colonies, proving their etiologic rôle. (The number of streptococci colonies on the solid crystal violet mediums were compared with the number of staphylococcus colonies on ordinary solid mediums and a much greater number of the former were found.) In impetigo bullosa the opinion of Jadassohn was confirmed, that is, that it is due to the staphylococcus. Also pemphigus neonatorum was found due to the staphylococcus. In the retroauricular and other kinds of intertrigo, characterized by deep fissures, Haxthausen found the streptococcus in great numbers, while the superficial forms showed only isolated colonies; in these yeast or other fungi were often found. In "pityriasis simplex" (dartre volante) of the face in children, described by Sabouraud as contagious and of streptococcal etiology, the author found numerous streptococcus colonies. Also in cases of pityriasis corporis, located especially on the lateral parts of the body, often complicated by intertrigo, most often numerous streptococcus colonies were found. In other cases ("dermatosis mediothoracica" and "pityriasis circinata") results were negative. In the well developed "seborrheic eczema" of the scalp, and of the more or less circumscribed patches of "seborrheic eczema" of the body, he found abundant colonies of streptococci. He concludes, that certain cases of so-called "eczema seborrhoicum" and "eczematide" can be attached to the category of "pityrisis simplex" ("dartre volante") of the face, and classified under "Pityriasis streptogenes." But in most cases of the seborrheic type of lesion the author believes that the streptococcus infection is not an etiologic factor, but of certain importance in the evolution of the lesion.

DAVID BLOOM, New York.

ALTERNATION OF DISEASES IN DERMATOLOGY. L. BROCQ, Ann. de dermat. et syph. **9**:1 (Jan.) 1928.

During his many years of practice, Brocq has been struck by certain cases in which cutaneous diseases alternate with visceral disorders. For example, he mentions instances in which infantile eczema disappeared while the patient had a bronchitis, and reappeared when the latter condition was cured. He also mentions a patient with eczema who was seen years ago and who became gravely ill with a malady diagnosed cerebral tumor. Brocq cured this patient by inducing a return of the eczema. Brocq briefly records a number of analogous cases and analyzes them. It is impossible to say what these curious alternations signify, but the knowledge that it exists may be made use of therapeutically in some instances.

THE RETICULO-ENDOTHELIAL TISSUE IN ITS NORMAL AND PATHOLOGIC STATES: A PROPOS OF A CASE OF URTICARIA PIGMENTOSA. HUDELO and CAILLIAU, Ann. de dermat. et syph. **9**:19 (Jan.) 1928.

This first memoir contains a detailed discussion of the reticulo-endothelial system. Following a short historical review, the authors present a general morphologic description of it, a discussion of its component parts and of its analogy to the reticular tissues of the viscera. The reticulo-endothelial tissue is not well developed in normal skin, but in some disorders (xanthoma, purpura, urticaria pigmentosa, etc.) it becomes greatly amplified.

SYPHILIS AND EXEMPTION FROM TAXES. J. AUDREY, Ann. de dermat. et syph. **9**:34 (Jan.) 1928.

For its historical interest, the author transcribes early sixteenth century tax records showing that the severe syphilis then ravaging France was the reason for the exemption of the afflicted from civic taxes.

PSORIASIS IN A NEGRO. P. NOEL, Ann. de dermat. et syph. **9**:37 (Jan.) 1928.

The author briefly summarizes the recorded cases of psoriasis in negroes. It is rare among full-blooded negroes. He reports a case in a middle-aged negro coolie.

THE PROPHYLAXIS AND THERAPY OF SYPHILIS WITH RUSSIAN PREPARATIONS OF STOVARSOL. N. EFRON and L. LIPSKEROV, Ann. de dermat. et syph. **9**:43 (Jan.) 1928.

The authors' researches on rabbits demonstrated that stovarsol introduced by the mouth eradicates experimental syphilis in these animals. From their clinical experience with this drug, they concluded that it possesses an energetic therapeutic action and approaches neoarsphenamine in efficiency. They did not encounter any ill effects from its employment. The poor results obtained by some investigators are ascribed to insufficient doses.

THE ETIOLOGY OF NICOLAS-FAVRE DISEASE: THE POSSIBLE PATHOGENICITY OF A VARIETY OF B. SUBTILIS IN THIS DISORDER. L. BORY, Bull. Soc. franç. de dermat. et syph. **35**:2, 1928.

Bory recalls the recent report of Kitchevatz concerning an organism found by the latter in this disease. About four years ago, Bory reported the finding of a bacillus in the disease, but this organism was apparently a variety of *B. subtilis*, and therefore he went no further in his investigation. He finds great similarity between Kitchevatz' and his own observations.

UNGUEAL MALFORMATIONS PROBABLY OF CONGENITAL SYPHILITIC ORIGIN. RAVAUT and MONNEROT-DUMAINE, Bull. Soc. franç. de dermat. et syph. **35**:9, 1928.

Two cases are reported of partial absence and malformations of the nails of the hands and feet. The syphilitic origin of the condition was not proved but was plausible.

ALOPECIA AREATA AND HYPERTRICHOSIS. LOUSTE, LEVY-FRANCKEL and JUSTER, Bull. Soc. franç. de dermat. et syph. **35**:12, 1928.

Several cases of association of pelade and hypertrichosis are reported. Three of the patients were women, one a man. The authors believe the association was adventitious.

LOCAL TREATMENT OF LICHEN PLANUS BY ULTRAVIOLET LIGHT. JUSTER and TCHIPROUT, Bull. Soc. franç. de dermat. et syph. **35**:15, 1928.

Ultraviolet irradiations in doses sufficient to produce erythema caused the disappearance of lichen planus in the irradiated areas, according to the authors' experience. This treatment may be combined advantageously with spinal roentgenotherapy.

A CASE OF PROGRESSIVE PIGMENTATION PROBABLY OF NEVOID TYPE. A. SÉZARY, M. DUCOURTIOUX and L. GALLERAND, Bull. Soc. franç. de dermat. et syph. **35**:16, 1928.

The patient had a flat pigmented nevus which began to extend about the time of puberty; the pigmentation appeared in reticulated and sheetlike forms. There was no endocrinous or other systemic disturbance to account for its extension; nor were there symptoms suggesting neurofibromatosus. Progressive pigmentation of the type presented is rare, and the literature on it sparse.

MICKULICZ' SYNDROME IN A SYPHILITIC PATIENT. JEANSELME, L. HUET and DESBROUSSES, Bull. Soc. franç. de dermat. et syph. **35**:20, 1928.

The patient had tertiary syphilis as well as difficulty in speech, macroglossia, macrocheilia, and enlargement of the parotid glands. The syphilitic infection dated back twenty-five years; the syndrome of Mickulicz, eight years. While other causes may produce this syndrome, the presenters regarded their case as due to syphilis.

HYPERTHYROIDISM AND ITS ACTION ON THE PILOUS SYSTEM. P. SAINTON, M. MAXIMIN and H. MAMOU, Bull. Soc. franç. de dermat. et syph. **35**:22, 1928.

The authors state that disorders of the hair are well known in hyperthryoidism. They present some studies of the influence of thyroid extract (in various forms) on the plumage of fowls and the fur of rabbits.

In hens, the feeding and injection of thyroid preparations lead to areate depigmentation and defluvium of the plumage. In rabbits, the same preparations lead to more diffuse decoloration and fall of hair. The effect obtained depended on the dose administered. Applying these results to human beings and adding thereto certain clinical experiences, the authors conclude that the thyroid origin of vitiligo is a justifiable hypothesis in some cases.

EXPERIMENTAL INVESTIGATIONS ON THE PREVENTION OF SYPHILITIC INFECTION BY THE USE OF TELLURIUM AND OF BISMUTH. C. LEVADITI, Bull. Soc. franç. de dermat et syph. **35**:28, 1928.

In view of recent reports in the French literature of the inefficacy of bismuth as a syphilitic prophylactic, Levaditi records some experimental work of his own on this question. Rabbits received one or two injections of a bismuth compound or tellurium, and after appropriate intervals attempts were made to inoculate syphilis by the subscrotal route. Tellurium was found efficacious, even in a single dose, but the degree and length of refractoriness of the animals depended on the dose and its speed of elimination. As to bismuth, its effect as a prophylactic was more profound and durable when administered as an insoluble salt rather than as the element itself. This metal is an effective prophylactic against syphilitic infection in rabbits if the dose is sufficient. Applying his experimental results to human infection, Levaditi said that the important factors are the dose and the salt of the metal used. The dose should be the same as that used in an "abortive cure;" an insoluble compound should be administered.

A MACULAR QUININE ERUPTION. C. SIMON, Bull. Soc. franç. de dermat. et syph. **35**:33, 1928.

Simon gives a brief report of a macular quinine exanthem.

A NEW CASE OF ARSENICAL STOMATITIS. C. SIMON and J. BRALEZ, Bull. Soc. franç. de dermat. et syph. **35**:34, 1928.

The authors have presented several cases of this nature. In the present case following several injections of neoarsphenamine, there developed gingivitis of moderate degree. This manifestation should be considered as a sign of arsenical intolerance and a precursor, at times, of grave complications.

PRESENTATION OF TWO MOULAGES OF CREEPING DISEASE. T. PHOTINOS, Bull. Soc. franç. de dermat. et syph. **35**:37, 1928.

The moulages were presented to the St. Louis Hospital collection. Illustrations show them to be taken from cases of striking multiple infestation.

ROENTGENOGRAPHIC STUDY OF PATIENTS TREATED BY INJECTIONS OF INSOLUBLE BISMUTH COMPOUNDS. A. GALLIOT, Bull. Soc. franç. de dermat. et syph. **35**:41, 1928.

Galliot took roentgenograms of twelve patients who had been given intragluteal injections of bismuth (various insoluble salts) about one year previously and found considerable deposits of that substance still present.

HIDRADENOMES ÉRUPTIFS. J. GATÉ, G. MASSIA and H. CHRISTY, Bull. Soc. franç. de dermat. et syph. **35**:48, 1928.

The disease appeared in this patient at the time of typhus fever. There was nothing unusual about the appearance of the skin disorder.

SEROLOGY OF PROSTITUTES (AT TOULOUSE). C. AUDRY and CHATELLIER, Bull. Soc. franç. de dermat. et syph. **35**:50, 1928.

Of 394 women examined, 187 gave a positive Wassermann reaction. Of those with a negative test, a great many had had previous treatment. Few showed clinical signs of syphilis.

BACTERIOLOGY AND SEROLOGIC INVESTIGATIONS IN PORADENITIS. M. KITCHEVATZ and V. KITCHEVATZ. Petrovich, Bull. Soc. franç. de dermat. et syph. **35**: 51, 1928.

The authors have previously described an organism obtained from a single case of this disease. Since then they have isolated it in three other cases. Complement-fixation tests were specific with this organism.

THE SPECIVITY OF ALLERGIC REACTIONS IN NICOLAS-FAVRE DISEASE. M. KITCHEVATZ, Bull. Soc. franç. de dermat et syph. **35**:53, 1928.

The author has previously presented an intradermic diagnostic test in this disease, employing an antigen obtained from material (by puncture) of the affected glands. He now presents more experience with it, confirming its specificity and differential diagnostic value.

MICHAEL, Houston, Texas.

SYPHILODERMA LUPIFORMIS. G. LANTERI, Arch. ital. di dermat., sif. **3**:3 (Oct.) 1927.

The author reports two cases of tertiary lesions in cases of congenital syphilis. In the first case, there was an ulcer which had destroyed the nasal septum and both nares. The patient was 21 years old, and the condition had been present for thirteen months. The second case was that of a child, aged 7, with scars and ulcers on the right side of the face and neck. In both cases, the clinical diagnosis had been lupus vulgaris. Antisyphilitic treatment cleared up the lesions in both patients.

MODE OF REACTION OF THE HUMAN SKIN. P. A. MEINERI, Arch. ital. di dermat., sif. **3**:15 (Oct.) 1927.

Histologic examination of the skin of the leg, twenty-four hours after ultraviolet radiation, showed a cellular reaction composed of polymorphonuclears, whereas normal skin of the dorsum showed only lymphocytic infiltration. Blood taken from normal skin of the back, twenty-four hours after irradiation of the leg with ultraviolet rays showed an increase of lymphocytes. Blood taken from the irradiated skin showed an increase in polymorphonuclears. Serum obtained from the irradiated skin showed a lower albumin content than serum taken from normal skin.

URICACIDEMIA, GLYCEMIA AND CHLOREMIA AFTER INJECTIONS OF CALCIUM. E. CIAMBELLOT, Arch. ital. di dermat., sif. **3**:42 (Oct.) 1927.

Immediately after intravenous injections of large quantities of calcium salts, the uric acid content of the blood is greatly reduced when the uric acid content was high, but it remains unaffected in normal cases. Sugar and chlorine also show a tendency to diminish after injections of calcium, especially when they are high above the normal. Improvement in some dermatosis following injections of calcium salts is in direct proportion to the reduction of the uric acid and sugar content of the blood.

NICOLLES' VACCINE IN THE TREATMENT OF CHANCROID. ITALO LEVY, Arch. ital. di dermat., sif. **3**:101 (Dec.) 1927.

The author reports his experience in the treatment of eighty patients who had chancroid, with Nicolle's vaccine intravenously, intramuscularly and subcutaneously. The best results were obtained with the intravenous injection. Febrile reactions were severe, but the clinical results were rapid, and healing of the lesions took place in a few days, without local treatment. Buboes resolved and disappeared without suppuration, and in case of ulcers, these healed promptly. The author concludes that Nicolle's vaccine is specific in the treatment of chancroid and its complications.

BOWEN'S DISEASE OF THE GLANS PENIS. T. SCOMMAZONI, Gior. ital. di dermat. e. sifil. **68**:1505 (Dec.) 1927.

This is a report of three cases of Bowen's disease of the glans penis and of the internal surface of the prepuce. The duration of the disease varied from two to thirty years. Clinically, the condition was a reddish, round, well defined patch, slightly squamous and somewhat infiltrated and elevated in places. Histologically, the three cases showed preepitheliomatous changes and beginning malignant degeneration. Dyscheratotic bodies were found and also atypical cornification. In one case, epithelial degeneration was obviously present.

APLASIA MONILIFORMIS. MARIO ARTOM, Gior. ital. di dermat. e sifil. **68**:1547 (Dec.) 1927.

The patient was a child, aged 9, who presented the hair dystrophy since the fifth month of life. The father and grandfather also had the same condition. None of the female relatives was affected. The hair dystrophy was accompanied by a marked keratosis pilaris of the neck and limbs. According to the author, the condition is due to a hereditary endocrinous disturbance. Capillaroscopic examination did not show alteration of the circulation of the scalp. The administration of thyroid gland produced some improvement at first, but later the condition remained stationary. Depilation with thallium acetate also failed, the hair showing the same dystrophy after its regrowth.

THE ALKALINE RESERVE OF THE BLOOD IN CERTAIN DERMATOSIS. U. Cerchiai, Gior. ital. di dermat. e sifil. **68**:1570 (Dec.) 1927.

Investigating the acid-basic equilibrium in the blood, the author finds that in most cases of eczema and psoriasis there is a slight acidosis.

PARDO-CASTELLO, Havana.

INVESTIGATIONS OF CUTANEOUS REACTIONS IN SKIN DISEASES. H. Haxthausen, Arch. f. Dermat. u. Syph. **151**:85, 1926 (Congress report).

The author has tested 200 cases by the scarification method, using 40 different extracts of food and clothing material. The extracts were prepared according to the original American methods, but by trying out several variations of each

extract on patients, who reacted positively, his associate Dr. Baagoe, succeeded in getting highly potent preparations which gave stronger positive reactions than the English or American extracts on the market. They also gave far less doubtful reactions; reactions principally in one certain group of skin diseases, in contrast to the preparations on the market, positive reactions in many skin diseases.

Most positive reactions gave cases of prurigo Besnier, which is identical with "spetexsudatives eczematoid" of Keller. Next in regard to frequent and positive reactions were cases of infantile eczema, in which itching was a prominent and a primary symptom. The urticarias gave, in contrast to the observations of most American investigators, a positive reaction only occasionally, the same as strofulus and eczema of adults. The reactions in cases of prurigo of Besnier and itching infantile eczema were mostly strong and in most cases multiple, as a rule, reacting at the same time to extracts of different hairs or of different grain. The principal kinds of extracts giving positive reactions were the extracts of different hairs, feathers, scales, grain, white of egg and yolk of egg (infantile eczema principally reacting to the last two). Never did one extract react in all positive cases, although human scales frequently produced positive reactions. His investigations make him conclude that there is no direct etiologic relation between prurigo Besnier, pruriginous infantile eczema and the material which produces the reaction, in contrast to urticaria, in which an etiologic relation is undisputable. He believes that the hypersensitiveness in the two former diseases are of different nature than real anaphylaxis. At present a positive reaction is to be considered only as symptom of a yet unknown and perhaps different condition of hypersensitiveness. The investigations justify and consideration of prurigo of Besnier as an independent disease entity, and they may be of help in the classification of infantile eczema.

A Case of Light Eruption, Resembling Hydroa Aestivale in a Patient with Hematoporphyrinuria, Produced by Phenobarbital. H. Haxthausen, Dermat. Wchnschr. **84**:827 (June) 1927.

The author cites a case of a young man, who, having been treated for epilepsy with phenobarbital, developed bullous eruption on the face and hands, after exposing himself considerably during the preceding several days to outdoor sunshine. The urine was of portwine color and contained hematoporphyrin. The nature of the eruption, the location, the hyperpigmentation of the skin between the lesions and the hypertrichosis resembled considerably certain forms of hydroa aestivale. This is the only case in the literature of "toxic hematoporphyinuria," associated with typical hypersensitiveness to light.

David Bloom, New York.

Paget's Disease of the Nipple. J. Mestschanski, Dermat. Wchnschr., **86**:173 (Feb. 4) 1928.

Mestschanski reports eight cases in which the clinical diagnosis of Paget's disease had been made. In one of these, histologic examination showed only harmless inflammatory infiltration; in another, only atypical proliferation of the lactiferous ducts. In the remaining six, true carcinoma was found, proceeding from the epidermis or from the lactiferous ducts or lacteal glands. Two of these patients had true skin cancer, not even clinically Paget's disease. One of the Paget lesions represented the transition stage to carcinoma, or "beginning cancer," which, it is impossible to say. Paget's cells may be seen wherever the nutrition of the epidermis is disturbed. In Paget's disease they are abundant, but they are sometimes present in simple proliferations of the lactiferous ducts and, more frequently, in ordinary cancer. The author believes that they are degenerated, vacuolated epithelial cells, sprung from the basal or prickly cell layers, but by no means cancer cells.

Dermatofibrosis Lenticularis Disseminata and Osteopathia Condensans Disseminata. A. Buschke and H. Ollendorff, Dermat. Wchnschr. **86**:257 (Feb. 25) 1928.

Buschke and Ollendorff found disseminated, oval or round, slightly elevated efflorescences on symmetrical portions of the skin in a patient in whom an anomaly of the bones was also present. This anomaly, discovered roentgenologically, consisted of disseminated, lentil-sized areas of condensation, located chiefly in the spongy bone and epiphyses, and having their long axis always parallel to the long axis of the bone in which they were. This condition of the bone has been described in the literature four times, first, by Albers-Schönberg. In these reports, mention is not made of lesions of the skin. The present authors suggest that both conditions are due to a common cause, a constitutional anomaly.

Immunity After Herpes Zoster. M. Obermayer, Dermat. Wchnschr. **86**:297 (March 3) 1928.

Obermayer reports a case of typical lumbosacral herpes zoster which recurred at the same site eleven times in the course of three years. The patient was a physician, aged 32 and otherwise healthy. Most of the attacks followed sexual excesses, with an "incubation time" of from two to four days.

Carpenter, Chicago.

DERMATOLOGIC ABSTRACTS

The Journal of the American Medical Association

Torula Infection in Man. O. Berghausen, Ann. Int. Med. **1**:235 (Oct.) 1927.

A case of ulceration of the tongue is reported by Berghausen, in which *Torula histolytica* was isolated from the lesion. The marked skin reaction following the subcutaneous injection of a boiled aqueous extract of a culture of the organism indicates that a state of hypersensitiveness existed. Complications in the form of a mottled infiltration of the parenchyma of the lung and enlargement of the spleen were present. The blood culture was negative. Unfortunately, permission was not granted to perform a necropsy to determine the character of the lesion in the lungs and spleen. At no time was it possible to obtain a specimen of sputum to examine for tubercle bacilli. The patient had never worked in an atmosphere containing dust, so that the changes in the lung cannot be attributed to siderosis. Temporary improvement followed the employment of neoarsphenamine intravenously. Local antiseptic measures in the form of the various dyes, arsphenamine and sodium perborate were of no avail. The exposure to the roentgen ray and radium was followed by such a reaction that the patient did not care to have these repeated. No improvement followed their use. Quinine sulphate and sodium iodide internally over a prolonged period seemed to be of no benefit. Death was due to inanition, the patient steadily losing in weight and finally refusing food.

Treatment of Lupus Vulgaris. J. Beatty, Brit. M. J. **1**:47 (Jan. 14) 1928.

The application found most generally useful by Beatty in the treatment of lupus vulgaris is a potassium-phenol mixture. In a 4 cc. wide-mouthed sample bottle stoppered by a rubber cap is placed 2.5 cc. of a solution of potassium hydroxide (1 part to 2 parts of water) in which is suspended precipitated calcium carbonate (1 part), and 1.5 cc. of phenol (carbolic acid). A pencil of cotton-wool wrapped round the point of a forceps is dipped in the fluid and

the area rubbed. As the rubbing is continued, the lupus nodules start out as purple spots, and nodules not previously noted can be detected. When these purple spots are well marked, the application is stopped; if it is continued, the whole area will turn a purplish black. A piece of unmedicated lint is cut the size of the area of disease, and on this is placed a fairly thick coating of a paste consisting of equal parts of salicylic acid, sodium salicylate and cane sugar, with enough glycerin to make a soft paste. This is applied to the area treated and the whole covered with zinc oxide adhesive plaster, which overlaps for some distance on all sizes so as to make an impervious dressing. The application is repeated twice a week, in most cases for four weeks, though not so long in superficial cases. On the removal of the first dressing, a granulating surface is found, lupus nodules not being visible, but if the wound was allowed to heal some nodules would be found. Repetition of the treatment is therefore necessary, but after the first treatment, touching with the alkaline phenol or slight rubbing only is required. No sign of phenol poisoning has occurred. The treatment fails when the impervious dressing cannot be properly applied—for example, on the nose, or close to the eye. In these areas it must be supplemented by acid nitrate of mercury or another powerful caustic, or, perhaps, by ultraviolet rays. It does, however, prepare the way for these by reducing the number of nodules.

ADDISON'S DISEASE WITHOUT PIGMENTATION. D. G. GHRIST and L. G. ROWNTREE, Endocrinology **11**:589 (Nov.-Dec.) 1927.

Ghrist and Rowntree report a case of Addison's disease resulting from tuberculosis of the suprarenals in which the clinical course was typical in every respect, except for the absence of pigmentation. The course was rapidly and continuously downward. The patient was not benefited by epinephrine and suprarenal cortex but appeared, in fact, intolerant to them. The diagnosis was made clinically and was confirmed by pathologic examination. This case represents the first instance of Addison's disease without pigmentation confirmed pathologically in the Mayo Clinic, although more than seventy cases of Addison's disease have been observed.

BLOOD PICTURE IN PURPURA. N. ROSENTHAL, J. Lab. & Clin. Med. **13**:303 (Jan.) 1928.

Rosenthal studied the blood picture in various types of blood diseases accompanied by purpura. He divides these purpuras into three main groups: (1) purpura characterized by a diminution of the blood platelets with or without alteration of their functions; (2) purpura due to some change in the function of the platelets without a diminution of their number; (3) purpura due to changes in capillaries. The blood picture in the first is diagnostic in cases of acute and chronic thrombocytopenic purpura, acute and chronic aplastic anemias and symptomatic thrombocytopenic purpura. The second group, chronic hereditary thrombasthenic purpura, is rare. The third main group is purpura due to conditions which affect the capillaries. A classification is presented as a result of a systematic study of 172 cases showing purpura as a primary or secondary symptom.

INTRAVENOUS BROMOTHERAPY IN PRURITUS. A. SÉZARY, Bull. méd. **41**:1451 (Dec. 28-31) 1927.

Sézary had prepared ampules of 10 cc. of a sterilized solution of sodium bromide containing 10 Gm. of this compound per hundred cubic centimeters of a sodium chloride solution (7.5:1,000). Patients with pruritus received daily intravenous injections of from 10 to 15 cc. In all, twenty-nine persons were treated, and cure was effected in most of those in whom the dermatosis was not connected with a severe organic lesion. Intravenous bromotherapy acts not only through its sedative effect on the nervous system but sometimes by shock and sometimes by a modification of general biologic conditions.

Dermatosis of Canine and Feline Origin. Hudelo and Rabut, Paris méd. **64**:56 (Jan. 21) 1928.

Mange in the dog is usually caused by *Sarcoptes scabiei canis* and in the cat by *Notoedres minor cati*. The presence of the former in the human skin results in a pruritus accompanied by an eruption of papular vesicles. It is an eruption relatively discrete and is disseminated, attacking especially the anterior surface of the forearm, the abdominal wall and the internal surface of the thighs. The *Notoedres minor cati* causes an eruption beginning with a papule, sometimes like nettle rash, which soon is topped with a vesicle and after ten days is transformed into a typical papule of prurigo. It may be distinguished by its monomorphous aspect and by its distribution which is dependent on the usual places of contract with the cat. The eruption is accompanied by a pruritus more severe at night. Cat mange will heal of itself if the cause of the disease is removed. Mange of canine origin should be treated, as is human mange, by the classic friction or by Milian's treatment. Inflammations caused by the trichophyton seem to be more often due to the dog. Favus of animal origin is rare in man. In microsporias the eruption is present only or is most marked on the uncovered parts. It is composed of some rounded erythematosquamous elements but especially of highly inflammatory lesions. The treatment of ringworm caught from animals is the same as that of all epidermomycoses.

Dressings of Ointment on Muslin. C. Simon, Paris méd. **64**:68 (Jan. 21) 1928.

A thin piece of muslin covered with ointment is an excellent dressing for localized skin diseases, especially on the limbs. Simon used five different kinds of ointment muslins; zinc paste muslin, weak reducing ointment, strong reducing, very strong reducing ointment and yellow oxide of mercury ointment muslin, in cases of eczema, psoriasiform parakeratosis, psoriasis, impetigo. The ease of its use, its cleanlines and the results obtained seemed superior to those obtained with the same prepaartions used as simple ointments, pastes or plasters.

Blood Coagulation in Disease. V. Brasil, Brazil-med. **41**:1247 (Nov. 26) 1927.

In some diseases, such as syphilis, pemphigus, leishmaniasis and cancer, the coagulating power of blood serum was found to be considerably decreased. Increased coagulating power was noted in typhoid and plague. In still other conditions, such as hookworm disease and malaria, there was little change. In leprosy, the results were indefinite. Of the various substances tested, dextrose neoarsphenamine and tartar emetic proved to be inert. Others, such as bismuth, manganese, sodium, tapioca and calcium chloride, raised the coagulating power. Iron, copper, lead and a weak solution of mercuric chloride decreased it. Sodium citrate and sodium oxalate act peculiarly, as they increase the coagulating power in vivo in the serum, but they lower it in vitro in the plasma.

Aortic Aneurysm. J. R. Goyena and A. Dagino, Semana méd. **34**:1560 (Dec. 8) 1927.

In a patient with a history of syphilitic infection and a positive Wassermann test, an aortic aneurysm developed. The condition advanced, in spite of various methods of treatment, including mercurials. The case seemed desperate when injections of metallic bismuth were started. Improvement was almost immediate. The aneurysmal shadow also decreased in size and the Wassermann test became negative.

LOCAL INSULIN TREATMENT OF ULCERS. E. NATHAN and A. MUNK, Klin. Wchnschr. **6**:1747 (Sept. 10) 1927.

Nathan and Munk found that insulin in its solution fluid, the same solution fluid without addition of insulin, and, as well, a suitable acid solution dropped on ulcerations (especially torpid crural ulcers), occasioned a severe tissue reaction characterized by seedlike, bright red granulations; growth of epithelium was thereby stimulated. After some time, however, the decrease of the ulcer surface ceased. Insulin substance freshly dissolved in physiologic sodium chloride solution and dropped on the ulcer does not produce the same results. The cure observed by Adlersberg and Perutz in the local treatment of experimental ulcers and torpid crural ulcers with insulin was not, Nathan and Munk state, due to the action of insulin, but must be ascribed to the action of the acid fluid in which the insulin was dissolved. The stimulation of granulations may be looked on as an effect of acid.

MALARIA TREATMENT OF TABES. G. WÜLLENWEBER, München. med. Wchnschr. **74**:2056 (Dec. 2) 1927.

The patients in thirty unselected cases of tabes were treated with malaria by Wüllenweber. Clinical improvement was obtained in 87 per cent; improvement in the reactions of the cerebrospinal fluid, in 82 per cent. There were two deaths with symptoms of vasomotor collapse. In consideration of the relatively good prognosis as to life for tabetic patients as compared with general paralytic patients, malaria treatment is justified in the first named, Wüllenweber believes, only in strong persons, without pronounced aortitis, obesity or hypertonia. The two fatal cases in this series were complicated by aortitis. The gastric crises and lancinating pains in the lower extremities, which form the chief indications for malaria therapy, may be temporarily exacerbated by the fever to such an extent that the treatment can be continued only under an opiate.

DIAGNOSIS AND PROGNOSIS OF SYPHILITIC AORTIC DISEASES. H. SCHLESINGER, Wien. klin. Wchnschr. **41**:9 (Jan. 5) 1928.

The increase in mesaortitis in recent years is beyond question. Schlesinger says some statistics place this among the most frequent of syphilitic localizations. The ascending aorta is a favorite site. It is often combined with atheroma, and aneurysm is a frequent sequela. Insufficiency of the aortic valve, when not caused by endocarditis, is syphilitic in origin in the overwhelming majority of cases. A myocardiac process of syphilitic nature often accompanies the aortic changes. If the coronary arteries become involved, the phenomena of angina pectoris occurs. One third of the patients with syphilitic aortic disease have a negative Wassermann reaction. The prognosis depends much on localization, complications and the time of beginning treatment. In isolated disease of the ascending aorta, it may be relatively benign. Aortitis accompanying neurosyphilis is seldom dangerous. On the other hand, more than half of the patients with mesaortitis die of this lesion.

HERPES ZOSTER IN ANGINA PECTORIS. R. WERTHEIMER, Wien. klin. Wchnschr. **41**:26 (Jan. 5) 1928.

The location of the herpes zoster in this case was over the region of the heart, over the left scapula and on the ulnar side of the left arm. The patient described it as being almost identical with the skin areas to which the radiating pains of the angina pectoris (on the basis of a syphilitic mesaortitis) were projected. Obviously, involvement of the eighth cervical segment was responsible for the herpes zoster of the forearm and involvement of the second, third and fourth thoracic segments was responsible for the herpes zoster on the

anterior and posterior aspects of the thorax. A causal connection between the herpes zoster and the angina pectoris, Wertheimer thinks, cannot easily be denied.

CASE OF NEVUS CANCER OF VULVA. J. SAHLER, Zentralbl. f. Gynäk. **51**:2859 (Nov. 5) 1927.

Two cases of cancer of the vulva — in a mother and daughter, aged 56 and 28, respectively — are reported by Sahler. In the daughter the neoplasm developed on the site of a wart excised two years previously. The tumor itself was not pigmented, but the surrounding skin was melanotically discolored. The wart had been almost black in color, but had not been examined histologically. The tumor gave the impression of a pendulous fibroma. The tumor and adjacent structures were excised and about ten weeks later the patient died with symptoms of exudative pleuritis. Metastatic nodules, of various degrees of pigmentation, were found in large numbers in the brain, the pulmonary and parietal pleurae, the heart, parietal peritoneum, great omentum, ovaries, uterus, and thoracic vertebrae. In the mother the lesion took the form of a series of nodules, varying in size from a pea to a walnut, and resembling pointed condylomas. They were broad based and nowhere showed degeneration. They were situated in the region of the perineum and on the inner side of the labia majora. They had been noticed for a year. In the last few months they had grown rapidly and caused pain in standing and sitting. The involved structures were excised into healthy tissue, and the patient is well one year later.

RHINOSCLEROMA. O. G. KALIN, Odesskii Meditzinskii Jurnal, January-June, 1927, p. 307.

Kalin gives an extensive historical review of the subject and supplements it with his own observations. The following deductions are drawn: Rhinoscleroma is an infectious granuloma characterized by large round cells, hyaline formation and presence of an encapsulated bacillus described by Frisch. The specificity of the Frisch bacillus is supported by a number of immunobiologic reactions, such as agglutination, specific bactericidal property and Bordet-Gengou's complement reaction. The latter, he suggests, may be utilized as a diagnostic aid in more or less obscure cases. Experiments with animals suggest the infectious character of the lesion. Among the etiologic factors are a number of biochemical deviations from the normal, such as a marked increase of calcium in the blood and a relative increase of potassium. The protease of the nasal secretions is also increased. The similarity to ozena in this respect is pointed out. The author believes that the further study of the biochemical properties of the organism and of nasal secretions will elucidate the pathogenesis of this disease and lead to prophylactic measures.

Society Transactions

MANHATTAN DERMATOLOGICAL SOCIETY

Nov. 10, 1927

DR. LUDWIG OULMANN, *Chairman*

CHANCRE OF THE NECK. Presented by DR. PAROUNAGIAN.

An Italian, aged 18, a room steward on a steamer, was referred to the Bellevue Clinic on October 24, 1927, and presented at that time a circular, elevated lesion on the right side of the neck, on the anterior aspect. The duration of the lesion was said to be about three weeks. The glands on both sides of the neck were markedly swollen. The mode of infection could not be definitely explained, as the patient did not speak English. However, it was stated that the infection was the result of a cut by a safety razor which the patient had used. He had had local treatment, and repeated dark-field examinations were negative, though the Wassermann reaction was reported as four plus. The patient was placed under treatment which modified the lesions somewhat.

DISCUSSION

DR. BECHET: It is somewhat difficult for me to agree with the diagnosis as presented. This patient has a four plus Wassermann reaction. The lesion has beeen present sufficiently long for the development of a secondary eruption. The lymph nodes should also be somewhat larger.

DR. FOX: While it is possible that this lesion is a chancre, I agree with Dr. Bechet that the case is not proved. The local adenopathy is lacking, and there is no general glandular enlargement. While the patient has received some antisyphilitic treatment, I do not think it is sufficient to have caused complete disappearance of the adenopathy.

DR. GILMOUR: I agree with Dr. Fox that the glands should be much more enlarged.

DR. ROSEN: I would be inclined to agree with the diagnosis of primary lesion if the spirochetes were found. The isolated, cleancut ulcer with marked infiltration of the edges, even in the absence of definite glandular enlargement, would substantiate the diagnosis of chancre. We occasionally see primary lesions without marked involvement of the contiguous lymph glands.

DR. SATENSTEIN: To me there do not seem to be enough clinical data for a diagnosis of chancre. The amount and duration of treatment have not been enough to absorb entirely the adenopathy which was reported present when the patient was first seen. I would say that the diagnosis was not fully established and would suggest some other type of infection in a person with a positive Wassermann reaction, possibly a fungus infection. I would suggest further study of the case.

DR. PAROUNAGIAN: I saw this patient on Oct. 24, 1927, three weeks after the lesion on the neck had appeared. He then presented a circular, elevated and eroded lesion which was indurated (clinically, a typical chancre). The glands of the neck in the thyroid region were markedly swollen on both sides, which condition could be seen at a distance.

We made three dark-field examinations, with negative results. The ship's surgeon had applied antiseptics, which might explain the negative results of the dark-field examinations.

My original intention was to have presented this patient at the Academy Section a week ago before treatment had been instituted, but because the patient did not speak English, I did not succeed. Since then he has been given two injections of mercury salicylate and one of neoarsphenamine, which have modified the lesion and reduced the glands of the neck. If the patient had been seen prior to treatment, I am confident that no one would have disputed the diagnosis.

DERMATITIS MEDICAMENTOSA (PHENOLPHTHALEIN). Presented by DR. SCHEER.

A man, aged 36, born in Austria, a laundry man, said that he had six attacks of an eruption during the previous ten months similar to the one he showed on presentation. The duration of the last attack had been two weeks. The patient had been chronically constipated, had taken cathartics frequently and, except for mild silver protein which he had taken just prior to presentation, had not ingested phenolphthalein. On admission the patient presented vesicular eruptions on the lips and penis, which had faded away by the time of presentation. He presented sharp, defined violaceous plaques from ¼ to 2 inches (0.6 to 5 cm.) in diameter, on the trunk and extremities and between the fingers of one hand. These patches were itchy and scaled moderately. A week previous to presentation, he had taken phenolphthalein for three nights without reaction.

DISCUSSION

DR. ROSEN: I believe that we are dealing with a bullous type of erythema multiforme, which may be due to a number of causes, one of which is drugs. In this instance, it happens to be phenolphthalein. When speaking of the usual phenolphthalein eruption, we mean the erythema perstans type.

DR. BECHET: I agree with Dr. Rosen's idea about this case. One thing somewhat militating against the diagnosis is that an increase or aggravation of the eruptions does not occur with the administration of phenolphthalein. It is also unusual for phenolphthalein eruptions to be bullous.

DR. FOX: I agree with Dr. Rosen that this is an erythema multiforme type of eruption, though calling it by this name is far from making a diagnosis. I think it possible that this eruption might be due to phenolphthalein or to some other toxic cause. The fact that the lesions did not become active under subsequent administration of phenolphthalein is an argument against its being caused by that drug.

DR. GILMOUR: I think this is an erythema multiforme.

DR. WEISS: In regard to the fact that the ingestion of phenolphthalein did not bring out a new rash, I would say that when for allergic purposes one gives certain substances (for example, strawberries) to a patient afflicted with a strawberry rash in order to combat the anaphylactic symptoms, one finds after a certain length of time the patient remains free from such skin manifestations. And so it may be with this case; the patient is so surcharged with phenolphthalein that the administration of that drug for experimental purposes does not bring out any skin manifestation. This does not speak against the diagnosis of phenolphthalein eruption. A certain immunity is built up in the system against the further appearance of such lesions. Probably in six months from now, when the immunity has been lost, the patient may again have lesions caused by phenophthalein.

DR. ELLER: I am inclined to make the diagnosis of a phenolphthalein eruption in this case. I agree with Dr. Weiss that drug eruptions may not be increased by further administration of the drug. Thirty-five years ago Prince A. Morrow said that further use of a drug may or may not cause an exacerbation of a drug eruption. At times there may be a great flare-up, while the same drug may not cause a change in the same person. This is a question of idiosyncrasy, concerning which little is known.

DR. OULMANN: I think the lesions on the buttocks look like a phenolphthalein eruption. There is certainly a multiplicity of lesions in this case, which I regard as a case of phenolphthalein eruption. Bullous eruptions in these cases are not so rare.

DR. OCHS: I agree with the diagnosis originally mentioned by Dr. Scheer; this is certainly a phenolphthalein eruption.

PHENOLPHTHALEIN ERUPTION. Presented by DR. OCHS.

The patient, a male, presented a phenolphthalein eruption on admission. He said that he had taken phenolphthalein from time to time during the previous nine years and had had four or five attacks of an eruption. The lesions were more of a bluish-gray color than those usually seen, varying in tone from pinkish to dark black, and contained light areas which caused a mottled appearance. The lesions were unusually extensive, being located on the penis, anal region, the navel, the face and the back. Some of the latter were as large as the palm of an adult hand.

DISCUSSION

DR. FOX: This is one of the most striking cases of phenolphthalein eruption I have ever seen, and, with the intense pigmentation, presents a reticulated appearance. I do not think there is any evidence of atrophic changes in the skin, as was suggested in an informal discussion. The skin appears normal to me, except for the pigmentation.

DR. ELLER: In reference to this case, I should like to refer to a case presented by Dr. Fred Wise; a patient presented a phenolphthalein eruption, deeply pigmented with white areas between the pigmented areas, caused by phenolphthalein. The pigmentation, however, was not as dark as in this case.

DR. OCHS: This case is presented, not because of the phenolphthalein eruption, but on account of the peculiar mottling in this condition. I have seen quite a number of cases of phenolphthalein eruption, but never one like this. In daylight one would think of argyria; the lesions are dark blue, not black.

A CASE FOR DIAGNOSIS (LUPUS ERYTHEMATOSUS?). Presented by DR. PAROUNAGIAN.

A woman, aged 21, married, had developed an eruption on her face in May, 1927, which was superficial, slightly scaly in character, and itched somewhat. About the end of September, 1927, the patient gave birth to twins (five months). A generalized eruption developed about five days after the delivery, which was about six weeks previous to presentation. The eruption was maculopapular with a slight tendency toward scaling. The itching was slight and was mostly present on the extensor surfaces. The lesions were present on the palms also. There were numerous lesions on the hard palate, and some lesions had developed on the upper lip about one week previous to presentation. The gums were red and bled readily. Four Wassermann tests had been made. The first, the Kahn test, gave a two plus reaction; the second test, made by the health department, was reported as "doubtful"; the two last tests, performed at Bellevue Hospital, were both reported negative. A tentative diagnosis of disseminated lupus erythematosus was offered.

DISCUSSION

DR. ROSEN: I think this patient is suffering from the acute type of lupus erythematosus. She said that the lesions had begun on the face during the last few weeks prior to presentation and had made rapid progress, spreading all over the body. The lesions on the palms and fingers are especially characteristic; they are erythematous and telangiectatic, such as are often seen in the acute type of this disease.

This patient should be hospitalized, as she has a high temperature and probably has an associated endocarditis. At Mount Sinai Hospital I have seen a number

of similar cases, in which patients were admitted with a diagnosis of malignant endocarditis, or some other septic process, and in which the skin manifestations of acute lupus erythematosus developed. Most of these cases have a fatal termination.

DR. BECHET: I would like to suggest that Dr. Parounagian use gold thiosulphate in careful dosage in treating this patient.

DR. FOX: I agree with the diagnosis of lupus erythematosus disseminatus. The eruption is extensive, affecting a large area of the trunk, and the pinkish macules on the palms and palmar aspect of the fingers are certainly unusual. I do not think that all of these patients die in a comparatively short time of tuberculosis.

DR. SATENSTEIN: When a case is presented as disseminated lupus erythematosus, a distinction should be made between the disseminated fixed type and the disseminated acute type. The fixed type shows the microscopic characteristics of lupus erythematosus, while the acute type shows only inflammation.

ANGIOMA CAVERNOSUM. Presented by DR. OCHS.

An infant, aged 8 months, presented a nevus on the back of the knee, about 3 inches broad by 5 inches long (7 by 12 cm.), raised, red, and ulcerated in the center.

DISCUSSION

DR. SATENSTEIN: I saw two cases in which patients were treated by multiple puncture with actual cautery with brilliant results.

DR. MOUNT: My feeling is that radium is the best treatment to use in these cases.

DR. ELLER: I agree with Dr. Mount that radium is the treatment par excellence which ought to be used in this case. We can use carbon dioxide snow, endothermy and other procedures, but why not use the best method available? If there is any condition in which radium acts well, it is in elevated angiomas.

DR. OCHS: I would like to know whether any one has found a case in which spontaneous cure occurred.

DR. ELLER: I think it is dangerous to allow any raised angioma to heal by spontaneous involution, because the scarring is usually much more severe than that following radium treatment.

DR. FOX: I do not agree entirely with what Dr. Eller has said. I had previously expressed my opinion regarding the ultimate outcome of hemangiomas. Many of them, I think, disappear spontaneously, either following some traumatism or without such an occurrence. The condition is fairly common in children but rare in adults. Some of the cavernous angiomas which are not encapsulated continue to extend, and destroy surrounding tissue like an aneurysm. These should be treated without delay. I think all will agree that the best results in the treatment of hemangiomas, in general, have been obtained by radium.

DR. BECHET: In reference to the spontaneous healing of angiomas, I wish to recall a case, in a boy, aged 3, who had a large angioma involving the entire right orbital region. The eye was completely closed by a large cavernous angioma at least 3 to 4 inches (7 to 10 cm.) in diameter. The lesion was ulcerating at two or three points. The eyeball seemed to be dangerously affected, but an oculist to whom I referred the case stated that with the exception of a mild pustular infection, the eye was intact. I prescribed some wet dressings, and the patient did not return. About a year later, the father brought him in for some other skin condition. The angioma had entirely disappeared; other than a superficial atrophy and a mild telangiectasia, there was nothing left. I immediately ascribed this most excellent result to some dermatologic interference, most probably radium. To my astonishment nothing had been done, the ulcerative process had extended, and with its subsidence the entire angioma had disappeared. The remarkable cosmetic results were ascribed by the father to the wet dressings.

CHLOASMA. Presented by DR. OCHS.

A colored woman, aged 35, the mother of six children, said that until her last pregnancy she had been perfectly well, but during the last pregnancy large, deeply pigmented lesions had developed on the sides of both cheeks and over the nose. The lesions had remained but did not itch, scale or cause pain or burning.

BLASTOMYCOSIS. Presented by DR. OULMANN.

A man, aged 35, a cutter, had developed a crusted pustular lesion at the angle of the mouth on the left side when he was 8 months of age. Since then the patient had had constant treatment with salves and injections. The lesion at the angle of the mouth had disappeared, but on the middle of the chin there was a lesion which extended upward to the vermilion border, and was pretty well circumscribed, with a few isolated pustules at the margin. When the patient arrived two days prior to presentation, the lesion was covered with a crust under which a small amount of pus was discharging. There was a deep fissure in the middle and on the upper and lower part, and the lesion was vegetating and papillomatous. Smears were made which contained a fine mycelium with tiny spheres and a number of double contoured cells.

LUPUS ERYTHEMATOSUS TREATED WITH A GOLD COMPOUND (TWO CASES). Presented by DR. PAROUNAGIAN.

A man, aged 50, had been presented before the society on Oct. 12, 1926. The diagnosis was accepted by the majority present, and treatment was instituted with solid carbon dioxide. After several applications of snow, the condition almost disappeared, and after several weeks recurred in a more severe form than before. Thereupon, treatment with a gold compound was resorted to, commencing with 0.01 mg. and ending with 0.1 mg., from Aug. 9, 1927, until just prior to presentation; the patient receiving fourteen injections. The result was satisfactory; only a slight trace of the disease remained.

A man, aged 20, had developed lupus erythematosus when he was 6 years of age and had been seen and treated by a number of well known dermatologists by various methods, and had come under the care of the presentor in October, 1921. He had been presented before the Society at least twice previously. There were discoid lesions on the face and body. On Aug. 12, 1927, he had been given the first injection of a gold compound, 0.01 Gm. Gradually the dosage was increased to 0.1 Gm. given in weekly injections, thirteen injections in all being given. The patient was not cured, but there had been a substantial improvement.

DAVID L. SATENSTEIN, Secretary.

NEW YORK DERMATOLOGICAL SOCIETY

Regular Meeting, Nov. 22, 1927

JOHN E. LANE, M.D., *President*

TREATMENT IN CASES OF ERYTHEMA INDURATUM WITH GOLD THIOSULPHATE. Presented by DR. CLARK.

Mrs. J. W., a housewife, aged 43, born in the United States, began to have "lumps" on the calves of both legs thirteen years prior to presentation. These apparently appeared at intervals for about three years, and then the lesions began to show a tendency to break down. Since then the patient had had new tumors appearing constantly on the lower part of the legs, practically all of which would ulcerate, leaving scars. Many kinds of treatment that had been tried had failed.

When the patient was first seen eight months before presentation, examination showed an unusual amount of ulceration and scarring from active and old, healed lesions, mostly on the calves of both legs. The ulcerations were almost as numerous and extensive as one ever sees in this condition. The Wassermann test was negative, and symptoms of syphilis were not present.

Eight months prior to presentation the patient was given biweekly injections of 100 Mg. of a gold compound. After seven weeks of these injections, the patient developed a slight dryness and itching of the skin, and this treatment was stopped for three weeks; sodium thiosulphate was then given intravenously, with a prompt clearing up of the dry dermatitis. Injections of a gold compound were then resumed as there were still a few open ulcerations on both legs. This treatment was persisted in for four weeks, by which time all the lesions were healed, and have remained so.

DISCUSSION

DR. WHITEHOUSE: I was glad to see the patient and think that the treatment in this case shows a wonderful result. It confirms the results Dr. Bechet has obtained in other cases of similar type. I believe other investigators have not obtained results in cases of necrotic granuloma and some other types of tuberculids. I do not think it has any connection with lupus erythematosus. Lupus erythematosus is a toxic condition, but tuberculosis is only one of the causes; it may come from infected teeth or other toxic conditions which sensitize the skin, whereas erythema induratum is a tuberculous manifestation —that is my conception of the difference.

DR. FRASER: Cases of erythema induratum have been reported in which inoculation experiments have been successful. My own experiments were not successful, and I have not been able to demonstrate the tubercle bacillus in the lesions. The fact that this patient yielded so readily to the treatment with gold compound would seem to support the view that erythema induratum is not tuberculosis. The precise mode of action of the gold preparation in these cases is not known, but the fact that it is much more efficient in lupus erythematosus than in lupus vulgaris lends support to the view expressed by Dr. Whitehouse that the lesion of lupus erythematosus is not tuberculosis. If lupus erythematosus is caused by either the tubercle bacillus or the toxins of that organism one should see more lupus erythematosus than one see accompanying chronic pulmonary tuberculosis.

DR. TRAUB: The fact that the condition in this case as well as in several others shown at the Academy, in which the patient had failed to respond to all other remedies, improved under treatment with a gold compound, does not lend proof of any association between lupus erythematosus and erythema induratum. That these conditions are often associated in the same patient is not denied. In many diseases the patients respond to treatment with arsenic, quinine and other drugs, affording no criterion for working out an etiologic basis on substantial grounds.

DR. RULISON: I am inclined to agree with Dr. Traub. A new drug is being tried in a great many conditions, and it is interesting to see in how many conditions the patients respond to it, although this does not mean that the conditions are necessarily related.

DR. WILLIAMS: As for the action of the drug, I do not know how it acts. It seems to be useful in many of these erythematous diseases and should be tried until its limitations are found. I agree with Dr. Traub that the fact that in several diseases the patients have been benefited does not mean that the conditions have any etiologic relation. The point has been made that there are several diseases grouped under the term erythema induratum, and also different cases of lupus erythematosus have apparently different causes; the exact etiology of this is unknown. I have seen a case of lupus erythematosus

clinically, in which the patient benefited in a few days from mixed treatment. Erythema induratum is a toxic skin reaction, a reaction to a toxin which is probably but not necessarily bacterial. Cases have been reported that were a trichophytide of some kind, not bacterial. It is therefore probable that many cases reported as erythema induratum were tuberculous; some tuberculids, and some produced by other causes. Of these two groups of disease, it is likely that in some cases of lupus erythematosus and in some of erythema induratum the condition is produced by the same cause and might yield to the same treatment; others will not yield. The fact that patients with lupus vulgaris are not benefited from treatment with gold and sodium thiosulphate would seem to indicate that this drug causes its effects in some manner other than by action on the tubercle bacillus and that skin diseases which yield to it are not tuberculous but are due to some other cause.

DR. ELLER: I agree with Dr. Williams' remarks.

DR. BECHET: I have always believed that lupus erythematosus, erythema induration, the sarcoids and the papulonecrotic tuberculids all belonged to a group with a common etiologic factor, and that factor is tuberculosis or some condition allied to tuberculosis. The undisputed specific effect of gold therapy on this group serves to strengthen my opinion concerning their etiology. In 1920, Koch prevented the growth of the tubercle bacillus with dilutions as small as 1:1,000,000 of potassium gold cyanide, and the fact that gold therapy has given disappointing results in cases of pulmonary tuberculosis does not disprove the possibility that its specific effect in the tuberculid group is due to the fact that this group as a whole is due to some different or attenuated form of tuberculosis. This view is further strengthened by the different course and symptomatology between visceral tuberculosis and cutaneous tuberculosis. Dr. Clark's case is interesting, but mine was even more so, for besides the lesions of erythema induratum on the legs—fully as extensive as in Dr. Clark's case, the patient had from thirty to forty large papulonecrotic tuberculids on her hands and forearms. Both types disappeared under treatment with gold therapy, simultaneously, and have not recurred. I have had a case of lupus vulgaris of the small disseminate nodular type in which the condition cleared up entirely under treatment with gold therapy; on the other hand, in two cases of the ordinary type of lupus vulgaris the condition seemed unchanged by the treatment. A private patient now under treatment with gold and sodium thiosulphate had an extensive lupus erythematosus on the face and many sarcoid lesions of the Boeck type on the back and arms. The improvement has been most noticeable; several of the plaques of lupus erythematosus have disappeared entirely from the face, and the sarcoid lesions are greatly diminished in size.

DR. WISE: I am inclined to agree with Dr. Bechet's closing remarks. We have all seen patients with lupus erythematosus on the cheeks and sarcoid of the trunk, and lesions of erythema induratum on the calves in association with other forms of cutaneous tuberculosis. The two diseases appear frequently at the same time, and the patients are sometimes cured under treatment with gold solution. I would say that the two diseases are closely related and have much the same etiology; when the patient presents lupus erythematosus of the cheeks and coincident erythema induratum of the calf, no one would doubt that the relationship must be close, and I think the etiology is identical. I would say the same for sarcoid. In the case which Dr. Bechet mentioned—in which the patient had typical lupus erythematosus of the face and sarcoid of the body—this etiologic relationship seemed particularly striking. Dr. Eller said that he did not know of a case of lupus vulgaris in which the patient was cured by the treatment with a gold compound. That is not correct. Dr. Abramowitz recently presented a patient with widespread lupus vulgaris of the face and neck who had apparently been cured under treatment with a gold solution within a brief period.

Dr. Clark: The case brought out the discussion I desired. It seems that Dr. Whitehouse is inclined to believe that lupus erythematosus may or may not be a tuberculosis; Dr. Highman would be inclined to think that lupus erythematosus and erythema induratum might be tuberculoses; it would seem that Dr. Williams thinks that lupus erythematosus and erythema induratum might both be tuberculids and neither of them really a tuberculosis of the skin — so a variety of opinions has been expressed. I have talked with Dr. J. A. Miller, a recognized student of tuberculosis, and from the work he has done, and read, and had experience with, he has come to the conclusion that treatment with a gold compound is ineffective in pulmonary tuberculosis, in lupus vulgaris and in other typical tuberculoses of the body. The results are so scant that they are not enough to count in calling it an effective method of treating patients with tuberculosis — and apparently these various remedies have been discarded in the treatment of patients with frank tuberculous diseases. That may be taken for what it is worth. Erythema induratum is apparently distinctly influenced. I had four cases, and there are others that I know about in which the patients have been favorably benefited or cured by treatment with a gold solution. Lupus erythematosus is cured in from 80 to 100 per cent of patients treated with a gold compound.

Some one spoke of the various preparations. I think that it has been demonstrated that a gold compound is the least toxic of all the preparations, and much less so than sodium auro thiosulphate. In my work I rarely gain any more reaction than a mild dryness of the skin with a little itching which soon passes off when the treatment is stopped.

Dr. Wise brought out that lupus erythematosus and lupus vulgaris are sometimes found in the same patient and also sarcoid. Because they are present does not necessarily signify a similar etiologic factor. It is possible that they are coincidental. I mention this to show how the members of this society and dermatologists in general are up in doubt in regard to the tuberculids and tuberculosis of the skin.

Urticaria Pigmentosa. Presented by Dr. Schwartz.

Miss M. M., aged 24, presented discrete walnut-brown macules of urticaria pigmentosa, chiefly on the legs and buttocks, with a few lesions on the trunk. The duration of the lesions was eighteen months. The clinical diagnosis was confirmed by the microscopic observations.

DISCUSSION

The case was accepted as a typical one, by all the members.

Erythema ab Igne. Presented by Dr. Bechet.

B. S., a woman, aged 23, said that the eruption had been present for two years. It had disappeared almost entirely during the summer. The lesions occurred in annular and gyrate patches ranging in color from a deep red to purple; there was considerable pigmentation. The eruption occupied the inner side of the left leg and the outer side of the right leg. The patient did all of her work at a desk near a radiator, because of a cold office.

DISCUSSION

Dr. Fraser: The heat is not the sole cause of the clinical phenomenon. In a recent article, Dr. Williams pointed out the probability of the existence of a congenital defect in the blood vessels.

Dr. Bechet: I would like to ask Dr. Williams whether he considers livido reticulata allied to erythema ab igne.

DR. WILLIAMS: I think the whole group is dependent on some congenital anomaly brought to light by some exciting cause later in life—sometimes tuberculosis, sometimes syphilis, sometimes the sun or other factors.

BOWEN'S PRECANCEROUS DERMATOSIS. Presented by DR. RULISON.

Dr. A. N. G., a dentist, aged 48, married, was first seen Nov. 11, 1927. His parentage was German-American. There had been no family history of cancer, syphilis or tuberculosis.

From three to five years before presentation the first lesion had appeared on the outer side of the calf of the left leg. About two years later a lesion had developed on the left nipple and areola. Later, eleven or twelve small new lesions had developed on the upper part of the chest, shoulders and arms. There had been no sensory disturbance and no discomfort. There was no history of bleeding or oozing from any of the lesions.

The lesion on the left leg was round, dollar-sized, and covered with a thick verrucous crust. The underlying surface appeared a dull red. If the surface was papular it was so slightly so as to make such a characterization questionable. The lesion on the left breast involved the nipple and the entire areola. The nipple seemed to have flattened down to the level of the surrounding skin. The general appearance was that of a chronic scaling eczema.

The dozen smaller and more recent lesions were best described by Bowen in his second article in his resumé of Darier's description of his second case (Bowen's case four), as follows: "Red and scaling patches, sharply circumscribed, flat, level with the normal skin and covered with fine white adherent scales. The skin was neither thickened nor indurated, and seemed, on the contrary, slightly atrophic."

In the left axilla were several hard, small, discrete glands which were readily palpable. The right axilla seemed free from palpable glands.

Biopsy specimens were taken from the edges of the lesions on the leg and breast and from one of the newer lesions on the right side of the chest anteriorly. Dr. Daldorf reported the histologic observations as follows:

"The lesion is similar in all three tissues, consisting chiefly of changes in the epiderm, of an anaplastic nature. Giant cells, multinuclear forms (clumping forms of Bowen), mitotic figures — frequently much distorted — great disorder in cell arrangement and shape, as well as staining reaction, are found in all of our preparations.

"The 'corps rond' mentioned in the literature do not occur in the slides so far cut. An additional change in the specimen believed to be from the areola, shows a curious mucoid degeneration in the papillary body. Similar epidermal pictures are seen in carcinomata, as of the cervix uteri. I have found no direct evidence of malignancy. The case appears to belong to the group described by Bowen and named by him 'dermatitis precancerosa.'"

DISCUSSION

DR. HIGHMAN: Clinically, the patient looked as though he had multiple epitheliomas. The majority of the lesions looked like the ordinary basal cell, benign, rodent type. The locality of the two lesions on the nipple made one think of Paget's disease, even though the patient was a man. The lesion on the left calf did not look like the lesions Bowen described. The discussion should be divided into the clinical and microscopic aspects. Clinically, Bowen and Darier described seven such cases. When the late Dr. Johnston was with us, I had the good fortune to see a case at Cornell that had the features Bowen described. The lesions were grouped and without directly looking like a serpiginous syphiloderm, they nevertheless suggested it. The microscope revealed the type that this patient does. In Bowen's early case there was no evidence of malignancy; in his later cases, there was. In Darier's cases there was malignancy. Thus in seven cases of the eight, malignancy was found. Of

course, without referring to the absurdity of naming a disease precancerous when it is cancerous, one will have to be guided by the histologic aspects of the lesions. Histologically, in Bowen's dermatosis — even when evidence of epithelioma was not found — the changes in the epidermis were as outlined by Dr. Rulison in the present case. Similar if not identical observations can invariably be observed in Paget's disease of the nipple. Whether the clinical conception that Bowen first postulated in favor of the more striking and constant histologic symptoms of malignancy will have to be abandoned is a question for the future. But certainly it seems that one may call a case Bowen's dermatosis irrespective of its histologic aspects if it shows the required clinical features. This patient has epithelioma, so that it seems to me that it is time, perhaps, to relegate Bowen's entire conception to an interesting past, and frankly call these cases epithelioma of the skin with peculiar and constant epidermal observations under the microscope.

Dr. Williams: I agree with everything Dr. Highman has said, and would like to add one or two points. In many cases of epithelioma of the skin, there appears to be a period when histologically the typical changes are not present; and in many cases there are changes at the basal layer, sufficient to make a pathologic diagnosis, and this period may vary from a short period to several years. In the present case there is a long period before definite changes characteristic of malignancy can be discovered. Apparently in some cases, therefore, it is probable that a clinical diagnosis can be made before a histologic diagnosis. Some of these cases are apparently malignant or would be if left alone long enough.

Dr. Clark: I have reached the point where, after looking for a case of Bowen's type of dermatosis, I have made up my mind to forget Bowen's conception and call these lesions, as they are seen now, multiple flat epithelioma of the skin.

Dr. Eller: I agree with Dr. Highman and Dr. Williams that this condition should be called multiple flat epithelioma of the skin. We have all had experience with this type of epithelioma. It is not so responsive to the ordinary dosage of roentgen-ray or radium as is epithelioma of the cheek. I think the explanation is that there are not so many young cells, as the lesions may last for ten or twelve years, or longer. The older cells would be more resistant than the younger ones; so larger doses are required to cure multiple flat epitheliomas of the skin.

Dr. Schwartz: I agree with what the previous speakers have said about calling this condition multiple epithelioma of the skin. In my opinion, the most important question is what should be done for the lesion on the nipple. If I had that lesion, I would be worried, and the treatment that should be carried out is a matter for serious consideration. I believe that a radical operation, including careful dissection of the axilla, should be performed — this to be followed by deep roentgen-ray or radium therapy.

Dr. Wise: I also agree with the majority of the speakers that the lesions should be called multiple flat epitheliomas. Some of the lesions present the dyskeratotic changes in the epidermis. I had a patient with both nasal and squamous cell epithelioma on the body at the same time, but lost track of him; two years later, he was under observation for spinal cancer at the Memorial Hospital.

Dr. Fraser: One of the sections shows the structure of basal cell carcinoma: the other, a histologic picture practically identical with the cases described by Bowen. Paget's disease of the nipple and arsenical keratosis present a similar picture. In these cases the pathologic changes appear to be confined to the epiderm. They might be termed carcinoma in situ. With invasion of the dermis, they become infiltrating carcinomas. Radical excision would be my choice of treatment in Dr. Rulison's case.

DR. WISE: I agree with what Dr. Eller said about the remarkable obstinacy to roentgen-ray treatment of multiple flat epitheliomas of the skin. I have frequently removed the lesions with a knife.

DR. ELLER: I think a reasonably wide excision with the endotherm knife will be the best procedure, followed by sharp doses of roentgen rays or radium to the glands of the right axilla.

DR. HIGHMAN: He ought to have the glands dissected out, and the lesions destroyed by electro-coagulation and then treated with deep roentgen-ray therapy — also the scars where the other lesions are should be treated with the roentgen-ray.

DR. RULISON: I thought the case was of interest as possibly showing a combination of the so-called Bowen's precancerous dermatosis and Paget's disease. Apparently no one is using the term Bowen's disease when there is any evidence of malignancy; yet two of Darier's cases showed malignancy and one had a frank carcinoma of an axillary gland, and at the time of examination they were considered by Darier to be cases of Bowen's precancerous dermatosis. I can discuss this case from the standpoint of pathology only in the most general way, but my understanding is that in these two conditions — Paget's disease and Bowen's disease — there is a change in the skin which is somewhat characteristic; it is not of itself carcinoma but precedes carcinoma — and slides from this case do show this condition typically. If the term Bowen's disease is to be discarded and if all these cases are to be considered carcinoma of the skin, how is one to distinguish this type from those that fail to show such changes? I hardly see why this case should not be included under the Bowen's precancerous dermatosis group — if that remains in the dermatologic nomenclature. Several of the slides are typical. Darier's second case showed a multiplicity of lesions, and one of the type of lesions described coincides fairly well with the younger lesions in this case. In spite of the fact that these lesions vary from one to five years in duration, they are all similar histologically.

DR. WILLIAMS: I think we all agree that this is a case of Bowen's precancerous dermatosis, and that the lesion on the nipple may be Paget's disease. The entire discussion has been about terminology rather than about clinical facts. Bowen's precancerous dermatosis, or, simply Bowen's dermatosis, is a convenient term to distinguish a group of cases of long duration, many of the lesions of which, in their early stages, do not show any changes which can be recognized under the microscope as cancerous. It is probable that all the lesions show, ultimately, the microscopic changes characteristic of cancer, but the term is useful and should not be discarded.

REPORTS ON CASES PREVIOUSLY SHOWN.

DR. WISE reported that in the case of squamous cell epithelioma of the perineum, previously presented, the patient was under treatment with radium at the Memorial Hospital.

DR. RULISON reported that the case for diagnosis presented at the October meeting was still being studied, but that a diagnosis had not be made.

DR. FRASER said this patient had now some large ulcers.

DR. MALONEY reported that in the case shown at the October meeting as lichen nitidus with possible tuberculosis cutis, a histologic examination of the lesion on the hand, made by Dr. Highman confirmed the diagnosis of tuberculosis cutis. Dr. Highman also reported that the structure in certain superficial sections of this lesion resembled very much that found in the typical lichen nitidus lesions.

PAUL E. BECHET, M.D., Secretary.

ATLANTIC DERMATOLOGICAL CONFERENCE

Scientific Session, Philadelphia, Dec. 2, 1927

PATRICIA HART-DRANT, M.D., *Presiding*

PSEUDOPELLAGRA. Presented by DR. WEIDMAN.

W. McD., aged 46, white, a carpenter, presented generalized pigmentation of thirteen months' duration, least marked on the face, and most extensive on the extensor surfaces. The patient was mentally clear, but had a marked diarrhea.

Examination revealed: Wassermann test, negative; blood counts, normal; blood sugar, 113 and 71; blood urea, 8 and 12; sputum, negative for tuberculosis; feces, negative for parasites; roentgenograms of lungs and intestines, negative but suggestive for tuberculosis.

The patient was widely travelled. On admission, his temperature was 105 F.; his blood pressure was 120 systolic and 70 diastolic. At one time there was a pigmentary macule on the interdental line. The abdomen was tender and rigid.

Antidiarrheal treatment (bismuth) had been given and he had been placed on a high purin diet including liver. Other treatment had consisted of colloid baths; 5 grains of epinephrine three times a day, ultraviolet therapy and colonic irrigations with sodium bicarbonate.

The case was presented as pseudopellagra in a person who did not drink, and who was not on a monotonous diet.

DISCUSSION

DR. STOKES: I should like for Dr. Weidman to give a description of pseudopellagra since several men here would like to know what it is.

DR. WEIDMAN: The question has been thoroughly discussed in the literature of the last few months. Dr. Klauder and two or three others have written on the subject. As I understand it, nobody has decided that alcoholic pellagra is different from pseudopellagra, or that it should be known by any other terms. Patients with pseudopellagra, as a rule do not show a dementia and the condition does not follow the same course as characteristic pellagra. Persons who have it recover in a few weeks, spontaneously or on a simple hygienic regimen. It is in that sense that I used the term in the case under discussion. This case has continued for a longer time than the other cases of alcoholic pellagra or pseudopellagra which we had seen in the Philadelphia General Hospital. Perhaps tuberculosis is a factor in this patient's condition, for he has "suspicious" consolidations in the lungs. A tuberculous enteritis might upset assimilation and lead to the same end-result as in the surgical cases at the Mayo Clinic; esophageal cancer and old gastro-enterostomies led to obstruction, and this led to pellagra.

DR. STOKES: Is there not some suggestion of tuberculosis here? I think Dr. Klauder could elaborate on the subject of pseudopellagra much better than I could. The pigmentary phase, of course, is impressive, but I was disturbed by the nodule which the patient presents. I think that the one on the hand looked like tuberculosis verrucosa cutis. I had the impression that the man had more than pigmentary symptoms; the pigmentation was simply a part of the picture and not the principal condition.

DR. WILLIAMS, New York: I had the impression that the lesions on the backs of the hands were tuberculosis verrucosa cutis.

DR. SCHAMBERG: This patient was under my care during my service at the Philadelphia General Hospital. He presented a curious complex of symptoms. At one time the verrucous appearance of his hands was not present.

The buccal mucous membranes showed distinct brownish patches similar to those seen in Addison's disease. He had asthenia and protracted diarrhea for many months. There were symptoms which suggested Addison's disease considerably. The peculiar verrucous condition which has appeared since is something extraneous to that. I think that the diagnosis is far from being definitely established.

DR. STOKES: At the Mayo Clinic, I think that in two of the three or four cases which I saw, the condition was characteristic of pellagra. It was not pellagroid but distinctly pellagra, and I recall particularly that the picture on the backs of the hands coincided with the textbook illustration of pellagra.

DR. KLAUDER: I have seen a considerable number of patients at the Philadelphia General Hospital with pellagra following long alcoholic addiction. Some patients have presented a diffuse pigmentation similar to that of the patient in question. That, together with the asthenia, would simulate Addison's disease. It is only in that regard that the patient is entitled to the diagnosis of pseudopellagra. I do not appreciate the term "pseudopellagra." Why not speak of pseudo-Addisonian disease? It is pellagroid, but so are many other conditions. A patient with pigmentation may be pellagroid. I think the diagnosis of Addison's disease in this case is more logical. If this man has tuberculosis it is possible he also has tuberculosis of the suprarenal gland.

DR. WEIDMAN: In one case of true pellagra, from an insane asylum and in which I performed an autopsy, keratoses on the backs of the hands were sectioned and they did not show that the microscopic picture was that of tuberculosis. Keratoses are among the features of pellagra. I have photographs and lantern slides which show this striking occurrence.

DERMATITIS HERPETIFORMIS OR ERYTHEMA MULTIFORME PERSTANS. Presented by DR. WEIDMAN.

A. R., aged 41, a Polish kitchen helper, presented an eruption of five months' duration around the neck, extending onto the chest, on the forearms and over the sternum. The eruption consisted of dull red, corn-sized edematous papules which tended to form circinate groups, leaving a deep pigment on involution. There was itching only when the lesions were handled.

The laboratory observations were: sputum, repeatedly negative for tuberculosis (twelve tests); Wassermann test, negative or weakly positive; eosinophils, 2 per cent; *Streptococcus viridans*, cultured in sputum; later, Bacillus *influenza* and Friedlanders; blood sugar, 113; blood urea, 13. The microscopic picture suggested dermatitis herpetiformis. The blood study showed an eosinophilia.

The patient had had bronchiectasis for nine years. Recently he had an allergy-like flare-up around the lesions of the skin with wheal formation. There was a faint dermographism; the tongue had been red and swollen, and there was no diarrhea. The right eyelid had been puffy.

Treatment had consisted of bacterins (sputum), local antipruritics, bronchoscopic drainage and medication, without permanent effect.

DISCUSSION

DR. STOKES: To those members present who may have attended the meetings of the Chicago Dermatological Society, this patient is the twin brother, in the morphology of the lesion, of one of the cases shown there year after year to illustrate the evolution and regression of chronic erythema multiforme. At one time this case was diagnosed pemphigus. When the late Dr. Frederick G. Harris presented it at a later meeting of the Chicago Dermatological Society, he called the attention of the members to the fact that at various times they had diagnosed it as erythema multiforme, dermatitis herpetiformis

and pemphigus. The diagnosis of chronic erythema multiforme is probably as good as any that could be offered.

DR. WILLIAMS: This case is interesting in connection with another case presented in the same room — a case for diagnosis. The man also had lesions on the thighs. The second case was presented as chronic erythema multiforme, but the patient gave a history of having had an allergy-like flare-up around the lesions of the skin with wheal formation, which is not at all common in this disease. The general appearance, together with the hypertrophy, as if there had been granulation tissue, was still more suggestive to me of pemphigus vegetans, and that may be the diagnosis. On examination, it is impossible to distinguish between certain forms of erythema multiforme bullosum, dermatitis herpetiformis and some types of lupus erythematosus. There are mixed cases in which one cannot tell the difference at first sight, but after seeing this case and discussing it with the other men, I should be inclined to favor a diagnosis of pemphigus.

DR. WEIDMAN: The diagnosis that will probably appeal to one depends on the kind of eyes he looks through. If he looks through eyes of the Simon-pure clinician who will place more weight on subjective symptoms and clinical conditions, this is a case of Duhring's disease. On the other hand, the pathologic processes in the tissues showed that it was chronic erythema multiforme.

XANTHOMA TUBEROSUM MULTIPLEX, INVOLVING SCARS OF ZOSTER. Presented by DR. WEIDMAN.

W. M., aged 40, an Irish vendor, presented typical yellowish lesions characteristic of xanthoma on the palms, elbows, knees, flanks, chin and left side of the chest. Old scars on the scalp, and the vaccination and biopsy scars were not xanthic. The lesions on the left side of the chest were in the scars which resulted from a previous case of herpes zoster, and they followed the distribution exactly. There were no subjective symptoms.

The laboratory observations were: Wassermann reaction, 4 plus; blood cholesterol, 1,035 mg. (repeated examinations); blood sugar, normal. The histologic examinations showed xanthoma cells; the classic microscopic picture was that of xanthoma.

Other pertinent observations were enlargement of the liver and spleen, and jaundice.

Treatment had consisted of 20 doses of insulin; and 15 doses of iodopin without benefit.

The patient was presented because of the extreme blood cholesterol figure (highest ever recorded apparently); the deposit of cholesterol in fresh scars of zoster, but not in the old ones on the scalp and elsewhere, and the syphilitic basis for the hypercholesterolemia (?) with marked enlargement of the liver.

XANTHOMA TUBEROSUM. Presented by DRS. SCHAMBERG and WRIGHT.

G. T., aged 2, white, presented a generalized eruption of one and a half years' duration, consisting of hundreds of smooth lemon and orange colored tumors varying in size from that of a pea to that of a hickory nut. Some of them were brown.

The patient was presented because of the early onset of the disease and the enormous number of lesions for a child, aged 2.

XANTHOMA TUBEROSUM WITH JAUNDICE. Presented by DR. GITTINGS (by invitation).

B. B., aged 3, white, presented an eruption of xanthic lesions in a laparotomy scar, gums, eyelid and elsewhere. He had symptoms of terrible thirst and polyuria. Jaundice preceded the eruption.

The laboratory observations were: Vandenbergh test, immediate (direct); no urobilinuria; icterus index, 80; blood cholesterol, 120 mg.; sugar, 80 mg., and no parasites in the stool. The Wassermann test of that blood was negative. Roentgen-ray examination disclosed normal pituitary fossa and pylorospasm. The blood count was negative except for a polymorphonuclear count of 15,000. Biopsy of the liver showed an early infectious cirrhosis.

Other pertinent observations consisted of an enormous liver. Exploratory laparotomy performed seven months prior to presentation did not show biliary obstruction; the liver was large, soft and nodular. The spleen was slightly enlarged. The teeth had been extracted on account of a possible infectious basis of the liver disease. Vincent's organisms were present. Roentgen-ray examination of the chest was negative. The spinal fluid was negative. The internal medical symptoms were of at least two years' duration; the dermatosis, only five months.

The treatment had included extraction of the teeth; and neoarsphenamine.

The patient was presented because of the xanthosis in the fresh scars (gums, laparotomy), but not in the old one (vaccination), and because of the cirrhosis of the liver.

DISCUSSION ON THE THIRD, FOURTH AND FIFTH CASES

DR. ELLER, New York: I should like to ask whether any one present has observed any therapeutic results from a low cholesterol diet in cases of xanthoma.

DR. WEIDMAN: Has any one observed benefit from the use of iodized oil in these cases?

DR. KETRON, Baltimore: I should like to say just one word about the little boy, in the fourth case with the lesions all over his face. The peculiar mahogany color of the lesions is interesting. It is an unusual feature to me for I have never seen a case of xanthoma tuberosum in which that mahogany tint was present. The mother said this color occurred only after treatment with the roentgen ray and ultraviolet light, and that was the only explanation she gave me. I was wondering whether the other members had noticed a mahogany color in cases of xanthoma. It was different from what I have seen in the average case.

DR. WISE, New York: I should like to mention a case of generalized xanthoma shown by Dr. Whitehouse some time ago, in which the patient apparently got well after treatment with iodized oil. The lesions also had the mahogany color that Dr. Ketron has just mentioned.

DR. GREENBAUM: May I ask Dr. Wise if he knows the composition of iodized oil?

DR. WISE: No, I am sorry I do not.

DR. GREENBAUM: In a case of generalized xanthoma which I presented some years ago I used iodine in large doses without effect. My impression is that iodized oil is an iodine compound and does not have any effect on xanthoma.

DR. WHITE, Buffalo: I saw a case of generalized xanthoma six months ago in which the blood cholesterol was not elevated.

DR. WEIDMAN: In respect to the fifth case I should like to add that this is one of the most thoroughly worked-up cases of xanthoma of which I have knowledge. Dr. Gittings has thrown a new light on these cases, and has determined that this child has an acute infectious cirrhosis of the liver. He has searched for foci of infection. He has found Vincent's organisms in the mouth and treatment has been directed against this. The mechanism of these cases is, of course, an interference with the function of the liver; the liver

is an important cholesterol agent. In the pathology of xanthoma one should think particularly of the capacity of various things to inflict harm on the liver, particularly the cases of xanthoma in which jaundice is present.

HEMORRHAGIC SARCOMA OF KAPOSI. Presented by DR. SIDLICK.

A. S., aged 68, a Russian tailor, presented small nodular and flat discrete lesions closely crowded together on the lower part of the left leg and the lower part of the left thigh. They had a purplish-black color, and were firm. There was some itching and disability.

The Wassermann test was negative, and a biopsy made July 24, showed the typical histologic picture of sarcoma.

The lesions first appeared thirty-five before presentation in the region of the ankle as an eczematous outbreak which developed nodules and gradually spread upward.

Treatment consisted of deep roentgen-ray therapy which resulted in marked improvement. A few new nodules have appeared in the region of the midthigh.

The striking feature of this case was its unilateral character.

A CASE FOR DIAGNOSIS. Presented by DR. CORSON.

R. F., aged 48, a white railroad employee, had an eruption confined to the head and neck, unassociated with subjective symptoms. The present disease began fifteen years prior to presentation as a small spot on the left side of the neck. It was red, practically uninfiltrated and without scales, and spread slowly, in a circular shape. Six years previous to presentation a similar area began on the right temple, and later developed on the right side of the forehead and left side of the cheek. There was no loss of hair. The margin was sharp, and in places there was a suggestion of a pearly border.

The results of the Wassermann test and fungus examinations were negative. The histologic examination did not show any diagnostic pathologic features.

DISCUSSION

DR. WISE: May I suggest a diagnosis of granuloma annulare.

SYRINGOCYSTOMA. Presented by DR. SCHAMBERG.

L. B., aged 23, an American negress, a waitress, presented an eruption on the abdomen, arms and thighs of one year's duration, unassociated with subjective symptoms. There were myriads of discrete, pinhead-sized, moderately firm dark brown papules scattered thickly over the anterior surface of the trunk and over the forearms. There was no scaling nor umbilication. The patient also had a pelvic abscess.

DISCUSSION

DR. SCHAMBERG: This patient recently presented herself in our clinic and the question arose as to diagnosis. Clinically there was no marked degree of inflammation. In spite of this, some of the student physicians suggested lichen planus. The condition appeared to be syringocystoma or epithelioma adenoides cysticum or one of the associated conditions. Microscopically, I think the picture confirms the diagnosis of syringocystoma. You will recall that there were scores of lesions over the trunk. I think that the case is interesting because of the hundreds of lesions present and their wide distribution over the chest and abdomen.

DR. WISE: Do I understand correctly that the microscopic section was shown at this meeting?

DR. SCHAMBERG: Yes, it was brought in late. I think Dr. Weidman, who saw the slide, confirmed the diagnosis.

DR. WEIDMAN: How frequently has this condition been seen in the negro race? I have seen it in only one negro man, and this is only the second time I have seen it in the race.

DR. EICHENLAUB, Washington: I have had two cases in negroes, the microscopic diagnosis of which was confirmed by Dr. Sutton.

DR. HIGHMAN, New York: This disease is not rare. It is only when the condition is in its extreme form that the patients present themselves at the clinic, and, on account of the relative infrequency with which the condition is seen, it is thought to be rather more uncommon. It seems that if all the patients in the wards of general hospitals who were not sent there for some special skin disease could be examined, the prevailing opinion concerning the rarity of this disease would have to be revised. I do not say that the condition under discussion is common, but I question whether it is rare. It also seems to me that the cases in negroes exceeded those in whites.

DR. EICHENLAUB: In the Veterans' Bureau Hospital at Washington, 3,000 examinations have been performed on white men up to the time of this meeting and not one case of syringocystoma has been found.

DR. WISE: I think that more than one white male in 3,000 has had syringocystoma in the parts of the world in which I have attended clinics. Perhaps the patients Dr. Eichenlaub mentioned in the Veterans' Bureau Hospital came from a locality in which the disease is rare.

DR. EICHENLAUB: These patients come from all over the country and not only Washington.

DR. OTTO FOERSTER, Milwaukee: The clinical diagnosis which I made on this case was syringocystoma. The condition was unusual in that the lesions were so uniform in size, rather small, and had a rather sharp upper margin, and the distribution was unusual. It occurred to me that the appearance of the lesions, if they were found on the arms, would make one want to exclude leiomyoma as one of the possibilities.

BLASTOMYCOSIS CUTIS. Presented by DR. STOKES.

J. L., aged 24, an American negro laborer, presented a lesion on the left side of the neck, of three years' duration. It followed a surgical glandular excision. The wound failed to heal and gradually increased in size, extending peripherally. There are no symptoms.

The laboratory observations were: The Wassermann test of the blood was negative four times. The smears demonstrated blastomycetes; the cultures were positive for blastomycosis and the biopsy showed a classic blastomycosis. Roentgen-ray examination of the chest was negative; the tuberculin test was positive.

Treatment had consisted of potassium iodide, with partial improvement one year prior to presentation. The patient then discontinued treatment and became worse. At the time of presentation he was receiving potassium iodide, orally.

The case was presented because of the rarity of blastomycosis in Pennsylvania, and because of the absence of miliary abscesses at all times observed.

DISCUSSION

DR. STOKES: I want to stress one point about this case. It does not require any clinical discussion. The condition almost cleared up once under treatment with potassium iodide. The case illustrates how persons who acquire the disease must keep up the treatment. Failure to do this is the reason that so few get well. Most persons stop treatment when the conspicuous lesion is gone. I think they have to continue potassium iodide for a year or two after the lesion is healed or they suffer recurrence.

FRAMBOESIA. Presented by DRS. SCHAMBERG and WRIGHT.

J. G., aged 37, a Spanish laborer, presented a dermatosis of the palms, soles, face and penis. There were painful lesions with foul odor. The lesions on the face were verrucous; on the palms, keratotic; and on the penis, a single eroded papule.

Myriads of spirochetes have been recovered on dark-field examination. Roentgenograms showed characteristic vacuoles in the metacarpal bones.

The patient was given neoarsphenamine, marked improvement resulting.

The case was presented because it is a rare dermatosis.

DISCUSSION

DR. SCHAMBERG: This case, as you recall, was one of yaws in the convalescent stage. It has been my fortune to see two cases of yaws here in Philadelphia. A considerable difference of opinion as to diagnosis existed in regard to both. The first case was presented by a distinguished dermatologist of this city as a case of syphilis — a perfectly pardonable error. The Wassermann reaction was strongly positive; numerous spirochetes were present in the local lesions; and rapid cure took place under the administration of the arsphenamines; all facts of which would provoke some thought of syphilis. It has seemed to me from the study of these cases that there are several points in the differentiation. In the case we studied some few years ago it was found that the spirochetes in these lesions were more resistant to stain than the *Spirocheta pallida,* and animal inoculation in rabbits could not be kept up in series as long as the syphilitic inoculation in rabbits. Histologically, yaws shows abscesses in the epidermis, some of which contain spirochetes. From the clinical standpoint, both cases had distinct fungous, warty lesions on the palms, soles and scalp, an appearance which one does not get in syphilis, and hyperkeratotic lesions on the hands. Another point is that these spongy, warty lesions, when examined under the microscope, show more spirochetes to the field than a secondary syphilid would. There were sometimes six or eight spirochetes to a dark-field examination. A point which requires study and on which the literature is not clear is how long it will take for the Wassermann reaction to become negative after two injections of arsphenamine, which are usually sufficient to clear up the eruption of yaws. In one of these cases of yaws, the Wassermann reaction gradually declined in some weeks and became negative after two injections. This would not occur in syphilis.

LUPUS ERYTHEMATOSUS AND VITILIGO. Presented by DR. STRAUSS.

A. F., aged 54, a Russian housewife, presented an eruption on the face, neck and hands, without subjective symptoms. Lupus erythematosus began on the forehead and cheeks six years before presentation. Treatment improved these patches temporarily. Two years later, the lupus erythematosus disappeared and a large area of depigmentation bordered by a dark brown margin supplanted it. At the same time vitiligo appeared on the hands. Later the lupus reappeared. Active pulmonary tuberculosis was present.

Gold administered intravenously had been beneficial to the lupus erythematosus and the vitiligo.

The point of interest in this case is that the spread of vitiligo had, on occasion, removed the lupus erythematosus.

A CASE FOR DIAGNOSIS. Presented by DR. DECKER.

D. M., aged 78, a white watchman, presented an eruption on both sides of the neck, of one year's duration. It is associated with occasional itching. The patient stated that both ears were frozen in 1884. One year before presentation a vesicular eruption began on the right side of the face and neck, and

became progressively worse. Vesicles had been present constantly, and occasionally bullae. Itching was moderate, but was usually worse after the vesicles had ruptured.

Various treatments had been given without result.

DISCUSSION

Dr. Ketron, Baltimore: I think one must follow a case of this type for a long time to get any definite evidence. I should like to suggest a diagnosis of recurrent herpes.

Chronic Tuberculosis of the Skin. Presented by Dr. Sidlick.

B. J., aged 36, an American, a negro scrubwoman, presented an eruption on the face and extremities of a year's duration.

The lesions started as white infiltrated spots later becoming fungating and elevated. The face is the main seat of the eruption.

Microscopic section showed the presence of numerous small foci made up of mononuclear cells and giant cells. The patient has a four plus Wassermann reaction.

The administration of neoarsphenamine was without results. The examination of the chest suggested tuberculosis. Roentgenograms showed lesions which were not clearcut but which were suggestive of syphilis in the left root area.

DISCUSSION

Dr. Strauss: I think the rather interesting point about this case is the fact that the lesions started as depigmented areas which had no induration. These patches next showed a slight induration, and then they assumed the form which was seen on the face. In the cases of this condition that are usual, the fungating lesions develop first and the white areas follow. This case began with the depigmented areas and then became fungated.

Dr. Wright: About two years ago I reported a similar case in a colored girl who developed areas of depigmentation in which there later appeared lichenoid papular lesions. Microscopic examination showed what looked like a lichenoid sarcoid at that time. Other than the histologic picture and the fact that the girl had a pulmonary condition, there was no basis for the diagnosis. I think it would me much easier to arrive at the diagnosis if these depigmented areas could be stained for tubercle bacilli immediately on their appearance. Kyrle was able to demonstrate the tubercle bacilli in cases of sarcoid if he could see the condition a year or so before it developed fully, when the lesions were merely areas of slight redness.

Lichen Scrofulosorum. Presented by Dr. Ludy.

A. B., aged 21, an American negress, presented an eruption on the thorax, sacral region, extremities and face, of two years' duration. The lesions began on the face, then on the elbow, and finally spread over the entire body — all this transpired in three months. At the time of presentation there were myriads of papules the size of a pinhead.

Roentgen-ray examination of the chest showed a diffuse tuberculosis of both lungs. The Wassermann reaction was negative. The hemoglobin was 75 per cent; red blood cells, 3,720,000. Other blood items were negative.

Local treatment was not administered. Tuberculotoxin antitoxin (Scheitlin) had been given since August, 1927. The patient has gained 20 pounds (9 Kg.), and over half of the lesions had disappeared.

DISCUSSION

Dr. Bechet, New York: I disagree with the diagnosis, not so much on account of the basic microscopic picture of the case, which is said to be tuberculous, but the lesion began on the face. This is a point somewhat in

favor of the disseminate type of tuberculosis rather than a typical lichen scrofulosorum. The lesions were too nodular for the ordinary type of lichen scrofulosorum. I would suggest a diagnosis of the miliary tuberculosis of the skin.

DR. HIGHMAN: I do not see why the distinction is made. Clinically, the case was tuberculosis, judging by the grouping arrangement of the lesions. The rest of the case fits in with the diagnosis presented. Even if there is any difference, what great accomplishment would there be in changing the name of the disease from one Latin term to another? I do not see any advantage.

DR. SIMPSON, Washington: It is not a matter of two different terms for the same disease. There is a considerable difference between the two conditions mentioned by Dr. Bechet.

DR. STROHM: In the case under discussion the patient has an infiltration of both lungs, a pulmonary tuberculosis and an enormous loss in weight. An examination of a section showed epithelioid cells but no bacilli in the lesions. The patient was treated with tuberculotoxin antitoxin, a preparation made by Scheitlin in Switzerland. This resulted in a gain of 20 pounds in weight and a disappearance of over half the lesions. Such results do not occur in cases of the ordinary type of tuberculosis.

DR. HIGHMAN: Whether the condition is lichen scrofulosorum or miliary tuberculosis, this patient does not look as if she were near death.

KERATODERMA BLENNORRHAGICUM. Presented by DR. MACKINNEY (by invitation).

H. A. F., aged 30, white, an American fireman, had contracted gonorrhea eight years before and again four years prior to presentation. At the time of the last infection he had sores on his feet that resembled boils; the right wrist swelled, then the elbows and knees. He was in bed for five months. His joints became fixed. He recovered and went to work, but the joints did not entirely regress. A new attack of gonorrhea began three months before examination and an acute flare-up of the condition of the joints occurred. At the time of presentation he had an arthritis with marked deformity of the elbows, wrists, fingers, ankles and knees. The hip was unaffected. He presented patches of dusky erythema on the heels, the ball of the foot, the right wrist, the palms, the toes and around the nails. Some nails, both of the fingers and the toes, were markedly thickened and dystrophic. On admission, there were thick, horny, barklike keratoses over the lesions and they were more numerous — around the ankles, for instance. Real keratoses were not present.

Laboratory observations were: Urine, negative; the blood count, normal, except for a slight anemia; the Wassermann test, negative; the gonococcus fixation test, negative, with positive smears; the blood sugar, 85, and the blood urea, 15.

Treatment had consisted of injections of Pregl's iodine into the prostate. The only local treatment that had been administered was magnesium sulphate solution, and at that, only on one side of the body.

MULTIPLE EPITHELIOMAS. Presented by DR. PFAHLER.

B. S., aged 57, white, an American contractor, presented an eruption scattered over the entire body at the time he sought treatment, although at present the lesions are chiefly cicatricial. Two years prior to presentation, the patient had a hundred or more typical epitheliomas.

Two small untreated lesions on the right arm showed histologically early basal cell carcinoma of the skin of the arm. A specimen from the posterior left shoulder showed squamous cell carcinoma, type 1. A third lesion on the ring finger of the left hand showed a combined basal cell, and squamous cell carcinoma.

Electrodesiccation and roentgen-ray treatment were employed with achievement of the present result, almost complete cure of all lesions.

DISCUSSION

DR. HIGHMAN: I think this is a significant case, in the first place, because of the variation of the epitheliomatous lesions, and secondly, because of their relative duration. The condition began when the man was still at the borderline of the cancer age. The histologic structures of the lesions ran the whole gamut of the disease so far as microscopic description goes — from the basal cell type of lesions, through the squamous and mixed types of lesions. The squamous cell lesion was found in areas beyond the axilla and resulted from excessive radiation. Would this factor modify epithelioma? I think it ought to be considered as throwing a possible light on the kind of irritation which may cause a metamorphosis from a less severe to a more severe type of epithelioma. With respect to frequency a more important question might be asked and I am eager to hear what Dr. Pfahler has to say.

DR. TRAUB, New York: I have never seen a basal cell epithelioma on the dorsum of the hand. They are almost invariably prickle cell lesions at the start. In areas of the axillae and on the hands and arms they should all be considered prickle cell epithelioma.

DR. GREENWOOD, Boston: The condition seems to me to be arsenical epithelioma. The patient gave a history of taking drops for some disease or other when a young man. The Cancer Commission in Boston has seen large numbers of epitheliomas following the indiscriminate use of a solution of potassium arsenite.

DR. PFAHLER: Answering the last question first, this patient did take drops. I could not learn what they were because the physician who treated him had died. However, he took the drops for the lesions; therefore, I think we must assume that the lesions were there before he took them; therefore, the drops did not cause the lesions. With reference to the squamous cell character of the lesions, I think that this squamous cell epithelioma was the same type that is found in all the cases with which I have had experience with scars produced by excessive radiation. I think this was an ordinary epithelioma developed in the scar of an excessive radiation, because the lesion was entirely within the scar tissue. It did not extend in from the edge as it might have if it were part of the original process. With regard to the lesion on the finger, none of the lesions on the hand were examined microscopically, but Dr. Eugene Case made a study of the vegetative growth on the finger and found both the basal cell and squamous cell type in that one region. Whether or not the other lesions on the hand were different from those in the specimen which I took from the other hand, which had not received radiation, I do not know. The man has a new lesion which has developed since I treated him, on the right side of his back, 3 or 4 mm. in diameter. It has the general appearance of all the other lesions scattered over his body.

TUBERCULOSIS CUTIS. Presented by DR. STOKES.

M. P., aged 26, an American negro, a garage worker, presented lesions of three years' duration on both sides of the neck extending onto the chest. The condition began as a slight symmetrical swelling, just below the edge of the mandible. It is tender on pressure. Multiple sinuses appeared about one year after onset. There has been a moderate persistent pustular discharge from the sinuses. The lesions are asymptomatic except for tenderness to pressure.

The laboratory observations were: Wassermann reaction, negative; urine, negative; roentgenogram of the mandible, negative; biopsy, a nonspecific chronic inflammation; smears and cultures, negative for actinomyces; inoculation of guinea-pig, positive for the tubercle bacillus; roentgenogram of the chest, negative.

Twelve injections of gold and sodium thiosulphate were given, each dose 100 mg., with 70 per cent improvement.

LICHEN SPINULOSUS. Presented by DRS. SCHAMBERG and WRIGHT.

S. R., aged 7, white, a Hebrew, presented an eruption on the arms and thighs consisting of grouped follicular spinous elevations unassociated with any inflammation, but accompanied by a mild pruritus.

Treatment had consisted of roentgen ray and quartz light therapy, thyroid extract and local applications with but little benefit.

PRENATAL SYPHILIS — INTERSTITIAL KERATITIS, OSTEOMYELITIS, OSTEITIS, OSTEOPERIOSTITIS, CHARCOT JOINT, HEPATITIS AND SPLENITIS. Presented by DR. STOKES.

T. M., aged 25, an American, white, presented malformations of bone in the mandible (both sides), left arm, left tibia and left hip, the latter being a Charcot joint. The spleen and liver were markedly enlarged. There was an interstitial keratitis and Hutchisonian teeth. The lesions of the bone were of two years' duration. The osteomyelitis followed trauma in each case.

The laboratory observations were: The Wassermann test of the blood, Kolmer 44, Kahn 444; spinal fluid examination, negative; urine, negative; blood urea, 13 mg. per hundred cubic centimeters; roentgenogram, as demonstrated; hemoglobin, 40 per cent; red blood cells, 2,900,000, white blood cells, 3,850; blood differential: polymorphonuclears 61 per cent, large lymphocytes 5, small lymphocytes 33, mononuclears, 1.

The Wassermann test of the mother's blood was Kolmer 44, Kahn 444.

The treatment consisted of small doses of bismuth and sodium iodide, intravenously.

The case was presented because of the rarity of this combination in a prenatal syphilitic at 25 years of age.

DISCUSSION

DR. STOKES: This boy is one of the best examples that I have seen of the disturbed age-development ratio in prenatal syphilis. The roentgenologists insisted that he has a Charcot joint. The left hip was apparently a satisfactory Charcot joint. There was considerable roentgenologic interest in the case owing to the presence of areas of cystic degeneration in the osteomyelitic tissues.

DR. ELLER, New York: I should like to hear from some of the members present about the question of the tubercle Carabelli on the first molar, which is being discussed considerably in New York. Have members of the Society found the condition in most cases of congenital syphilis, and have they found it in cases which they knew were not congenital syphilis?

DR. WEIDMAN: The spleen and liver in this patient are enlarged. This is a case of syphilis in which the spirochetes have infected the patient both cutaneously and viscerally. The organism is not purely of the dermatropic strain or of the organotropic strain. I have seen a case of extreme congenital syphilis which came to necropsy in which there were no lesions, either grossly or microscopically in any of the viscera; and yet there was most extensive ulceration of the skin and necrosis of the bone.

DR. DRANT: Will some one answer Dr. Eller's question?

DR. STOKES: Since the patient is mine I might say that a Carabelli tubercle is without significance. I have had members of my staff who have Carabelli tubercles, and while I do not have one myself, I know them to be extremely common. It has been conclusively demonstrated by at least two recent surveys that they have nothing to do with congenital syphilis.

LICHEN SPINULOSUS. Presented by DRS. SCHAMBERG and WRIGHT.

M. K., aged 19, a negress, presented a generalized dermatosis which she had had since childhood. Other pertinent observations included chronic salpingitis, early pregnancy and endocervicitis.

MORPHOEA. Presented by DR. BROWN.

F. K., aged 58, white, a German housewife, presented a condition on the neck and trunk of several years' duration. There were numerous ivory-colored macules on the upper part of the trunk and neck.

DISCUSSION

DR. HIGHMAN: I think the question as to whether a case of this sort is called a morphea or not depends on the definition of terms, and that in turn depends on how small a patch must be before it is called morphea. Taken on the scale of measurement which I have in mind, this has out-stripped the morphea stage and is actually a case of scleroderma, with the concomitant lesion on the neck, which I think will bear investigation because it roughly suggests pseudoxanthoma elasticum to me. The case is by no means typical. Microscopically, morphea, scleroderma and pseudoxanthoma elasticum are all diseases of the elastic tissue. There might possibly be a relation between pseudoxanthoma elasticum and the morphea and scleroderma groups. I hope Dr. Brown will have microscopic studies made and let us know about it at some future time.

DERMATITIS HERPETIFORMIS. Presented by DRS. KNOWLES and LUDY.

J. V., aged 14, white, an Italian, presented a universal eruption consisting of papules and vesicles with a tendency to grouping, and marked generalized pigmentation. There was moderate itching. The history was that this condition followed vaccination at the age of 5 years.

DISCUSSION

DR. WILLIAMS, New York City: Whether this condition is called dermatitis herpetiformis or some other name, depends on definition. I would not call it dermatitis herpetiformis, because I do not think that is the name for it. It corresponds in all features with the eruption known as postvaccinal pemphigoid eruption; or if you do not like the term pemphigoid, call it a bullous eruption, and then you are not associating it with any other disease. The eruption is said to have followed vaccination nine years before presentation. As far as I am aware that is the longest period during which any of these cases has been followed. Doctor Pusey followed a case for six years, and I have followed one for three or four years. If you make any effort to determine the course of postvaccinal eruptions you run against a stone wall. The patients either die or move out of the city. A few cases have been followed for months or years and the course of the condition is about the same. The original lesion is a wheal. Many of these cases look like urticaria at the start. Vesicles or bullae develop, occurring usually in groups. In the case under discussion they were so widely scattered that they were practically universal. The origin of the eruption is unknown. It may be secondary to vaccination, but the connection is not established. Dermatitis herpetiformis does not present these characteristics. The itching in this case was at one time severe but was moderate by the time of presentation. The eruption in this case was not like herpetiformis, but resembles the other group of eruptions. In the case that I followed, the eruption varied with and without treatment. It yielded best to arsenic, clearing up several times following its use. The boy in this case apparently has had arsenic. He said he has been treated with drops. I think he also shows arsenical pigmentation and beginning roughness and scaling of the arms, which may be an early case of keratosis. I think he will develop distinct arsenical dermatitis if allowed to continue treatment with arsenic. The patient that I followed developed a hard sclerodermatous skin. I hope Dr. Knowles will keep this patient under observation, and follow the course of the condition for a number of years,

then tell us the ultimate result. My own patient has moved from Vermont to Canada. I have some photographs, however.

It may be interesting to mention one feature of my own case for the social aspect. The boy was not cured. At one time he was taken to Montreal and treated by Father Andrews, who was said to be a monk. He prescribed "St. Jacob's oil," 1 drop, three times a day. The father said it was pure olive oil, and that a cure took place following its use. It was a mystery until we examined the boy and found the lesions still present where they had always been. It is interesting to observe the difference between the lay and professional standpoint of cure.

DR. SCHAMBERG: I have been interested for many years in these post-vaccinal eruptions. Some are bullous and classifiable as pemphigoid eruptions; some as dermatitis herpetiformis. I have seen cases in children in which arsenic would clear up the eruption with remarkable rapidity, and then if the treatment were stopped the eruption would again appear. I have observed two children in whom the lesions began rapidly to disappear under the administration of arsenic, and the youngsters finally got well. I cannot see any serious reason for objecting to the diagnosis of dermatitis herpetiformis in this case. The grouping, itching and vesicular nature of the eruption is characteristic of this disease. The origin of the eruption, as Dr. Williams said, is unknown. I agree with him that cases of postvaccinal eruptions rarely last as long as this. There are cases of dermatitis herpetiformis which last as long or longer. Their relation to vaccination is an interesting and obscure one.

URTICARIA PIGMENTOSA. Presented by DEPARTMENT OF DERMATOLOGY AND SYPHILOLOGY OF THE UNIVERSITY OF PENNSYLVANIA.

K. C., aged 26, white, an American housewife, presented pigmented macules on the trunk, extremities, face and neck of eight years' duration. They began as urticarial lesions followed by pigmentary deposition. The lesions occurred in attacks, many new lesions appearing suddenly. There was no pruritus.

The laboratory observations were: The repeated Wassermann test of blood, negative; urine, negative; blood count and differential, normal; blood urea, 3.4 mg. per hundred cubic centimeters; blood urea nitrogen, 9 mg. per hundred cubic centimeters; blood sugar, 0.111.

It is interesting that there was an absence of mast cells on examination of histologic sections.

LYMPHANGIOMA CIRCUMSCRIPTUM. Presented by DEPARTMENT OF DERMATOLOGY AND SYPHILOLOGY OF THE UNIVERSITY OF PENNSYLVANIA.

E. F., aged 28, an American negress, a housewife, presented a dermatosis on the vulva, mons veneris, left buttock and anal region, of four years' duration. The condition began as numerous, thick walled vesicles about the anus and gradually extended. The advancing border stopped about 1 inch from an old abdominal scar, but continued in other directions. A Wassermann test of the blood was positive three years before presentation. Following the test, about 50 intravenous injections of neoarsphenamine were given, but the lesions of the skin were not affected. There were no subjective symptoms.

The laboratory observations were: The Wassermann test of the blood was negative six times; the results of urinalysis were negative. Histologic sections showed dilated lymphatic spaces, bacteria and subacute inflammatory reaction; not neoplastic. Two or three of the lesions were punctured and a viscous fluid obtained.

DISCUSSION

DR. HIGHMAN: This case was peculiarly interesting to me because fifteen or sixteen years ago, under the mistaken idea of what esthiomine was, I published a paper in collaboration with other dermatologists of New York and later found that both the other dermatologists and I had read the literature

carelessly and that esthiomine is different from the condition we had in mind. The condition that Doctor Stine and I saw was a condition similar to the one presented. The patient had a great many lymphatic cysts in the same region as this patient but in the patient here there seemed to be more verrucous character than I saw in my patient. I do not think that these cases are really instances of lymphangioma circumscriptum, but I think that there is lymphatic stasis; whether peculiar to local circulatory disturbance or not, I do not know. But these are lymphatic cysts produced by the blocking of the lymphatic circulation, for what reason I do not know, causing a sort of cystic local elephantiasis. The condition is not classical, and I would like to hear further discussion.

DR. STOKES: I have never seen this patient until this afternoon. She is a classical example of the production of pseudolymphangioma circumscriptum, if I may use the term, by obstruction of the lymphatic system at some point in its return circulation. I shall send Dr. Weidman and Dr. Highman reprints of a case which I reported from the Mayo Clinic, in which the obstruction was tuberculous in origin. A tuberculous lymphadenitis obliterating the lymphatic return leads to this type of picture. I believe that is what ails this colored woman. She had a number of scrofulous scars on the neck. The process was of six or seven years' duration. There is a profuse, foul, vaginal discharge. The lesions about the anus suggest tuberculous condylomas. The vulvar lesions show the formation of vesicles, which is the result of lymphatic obstruction probably by the tuberculous process.

DR. KLAUDER: The patients whom I have seen in the past with a condition of this nature were treated with roentgen-ray or radium therapy. I have never seen any treated by other methods than radiotherapy. Perhaps a good method would be electrodesiccation. Good results were obtained from this in similar conditions. Probably the radioknife could also be used. This might be quicker, but I doubt if it would be superior.

DR. WEIDMAN: I agree to a certain extent with the members who have discussed the case as to its pathologic process, but I think the same remarks apply also to lymphangioma circumscriptum multiplex as classically described. The microscopic picture of the latter is not that of a neoplasm. It is not that of a lymphangioma. It is a lymphangiectasia. Surgical scars are common in cases of lymphangioma circumscriptum. All of the factors which have just been mentioned are present except that they occurred in a slightly different order. As far as the basic pathologic process is concerned, we are in agreement, the differences concerning only the order of the first lesion. As far as the ordinary clinical criteria are concerned, they are present in this patient. There is the surgical scar just above the lesions. There are the nodules, from which (when punctured) fluid escapes. It appears that the only difference between this and the classical cases is that in the cases seen by Dr. Stokes and Dr. Highman they went a little further and inquired into the particular agent which caused the condition.

DR. CHAMBERS: This patient has had a great deal of roentgen-ray therapy without result.

DR. HIGHMAN: I am not clear yet whether there is the agreement between Dr. Weidman and myself that he indicated. The type of lymphangioma circumscriptum with secondary trauma, I think, was recognized in the literature as a lymphangiectasis. There is a difference between the two according to my grasp of the literature. I think that although lymphangioma circumscriptum multiplex is simply and solely a lymphangiectasis and possibly a congenital one, it nevertheless has this difference from the other form (the form that Dr. Weidman and I have agreed about) that it arises without our knowing anything about it or being able to ascertain the preexisting injury to the tissue. There is somewhat of an analogy between the way it arises and the way syringoma arises in connection with the sweat cysts. It is a cystic

change with some embryologic disturbance of the lymph vessels in the area affected, but is not identical at all with the type presented. A distinction must be made.

Dr. Weidman: I must confess ignorance on the literary slants alluded to. Apparently it is a matter of subtle causation on the one hand, and definite causation on the other, whose justification I cannot see. Take keloids as an example. What is the difference between idiopathic keloid and the keloid that arises from local trauma? In the one case the cause of the tissue reaction is known and in the other it is not. The two types referred to, if I understand Dr. Highman correctly, would be the same except that more is known about one than about the other. I would be glad to have Dr. Highman tell me more about it.

Papulonecrotic Tuberculid. Presented by Dr. Munson.

T. B., aged 21, white, a French Canadian surveyor, presented a generalized eruption, unassociated with subjective symptoms. The eruption was of two years' duration. There has been successive involvement of the general surface of the body by destructive and grouped papulopustules.

Thirty-five doses of gold have been administered intravenously, together with ultraviolet radiation. The condition has improved considerably.

DISCUSSION

Dr. Eichenlaub: Is the patient getting a reaction from gold, or is it due to local treatment? The reason I ask is that the patient had a generalized erythema, and a fine scale, which did not look like an exfoliative reaction.

Lupus Erythematous. Presented by Dr. Strauss.

M. B., an American Negress, an actress, presented an eruption on the face and scalp. Lupus erythematosus began several years before presentation. The face was involved and much of the scalp was denuded and atrophic. Following the administration of gold intravenously there has been considerable regrowth of hair. The case has had an unusual progress, including the regrowth of hair.

DISCUSSION

Dr. Ketron, Baltimore: I should like to report briefly an unhappy result in a case of lupus erythematosus after the use of gold and sodium thiosulphate. It was something apparently unique, and it was extremely important that we know that such a thing may happen. The patient was a little boy with lupus erythematosus on his hands, the chronic type. He was observed for a year, and did not present any changes in the lesions. There were no acute features. He was 10 years of age. He was given 20 mg. of gold and sodium thiosulphate without any reaction. A week later he was given 40 mg. of gold and sodium thiosulphate without immediate reaction. The mother brought him back to see me three or four days afterward because of a beginning eruption on his face, neck, and an enlargement of the glands in the neck. He also showed some small white plaques in his mouth and beginning conjunctivitis. He had a slight fever. He was put in the hospital immediately. Three or four days later he developed a rash typical of bullous erythema multiforme. He had bullous macular lesions over his face; he developed an intense stomatitis; his lips were swollen and covered with blood crusts; nourishment was difficult; there was a purulent excretion about the eyes which was painful. The child had a day and night nurse. We did not know what was going to happen. I telephoned Dr. Schamberg, and at his suggestion we gave the patient sodium thiosulphate intravenously and lime water by mouth in as great quantities as he would take. We also tried to get him to take food. His temperature rose to 102 and 103 F. over a period of several days, but the worst condition

was that of his cornea and conjunctivae. He gradually improved, and at the time of this meeting his skin has practically cleared up. He has a mild subacute dermatitis over his hands. The unhappy feature is that the boy is totally blind. The cornea is ulcerated all over, and he cannot see. Whether the lowering of his resistance allowed secondary infection to take place or whether it was the toxic effect of the gold, we cannot tell. We found Vincent's organism in his mouth. We do not know the significance of that. We do not know whether or not it was a secondary infection. An eye specialist told me that the condition of the eye was hematogenous. Is it possible that the gold and sodium thiosulphate stirred up some internal infection which may have been the cause of the lupus erythematosus? I just wanted to report this case to let you know about this unfortunate accident which has resulted indirectly in total blindness.

DR. SCHAMBERG: This case reported by Dr. Ketron is a unique result from the use of gold. I do not recall that among the patients treated by Møllgard and others in Denmark any such complication occurred, even after enormous doses. Møllgard, in the treatment of tuberculosis, advocated doses of 100 mg., 500 mg., 1,000 mg. and even as much as 1,500 mg. A gram was not uncommonly given intravenously. The patients developed all sorts of toxic eruptions which he interpreted as tuberculin reactions. In our studies on animals, we have found that gold has a special affinity for the kidneys and spleen and also for the skin. After death in animals a good deal of the drug is found in these particular organs. To my knowledge there is no drug toward which there appears to be such a great variation of susceptibility in different patients. We have given one patient an aggregate of 15 Gm. during a year without any complications. I believe we ought to make our initial dose smaller than we originally advocated. No initial injection should be above 50 mg. In cases in which the lesions have been of only recent development it ought to be less.

DR. RULISON, New York: Two cases have recently come to my attention. The first one I did not see but I heard about it from another physician. It was a case of lupus erythematosus in which the patient was treated with gold and sodium thiosulphate; a retinitis developed shortly afterward. The other case that I think perhaps needs mentioning is one in which I successfully treated the patient for some time for an extensive lupus erythematosus with gold and sodium thiosulphate. The patient's treatment was interrupted and later resumed. Six or eight injections have been given in the last series. The last treatment was given in July. About two weeks before this meeting the patient again presented herself. She could not see anything out of one eye. The ophthalmologist reported that she had an embolus.

DR. BECHET, New York: I want to congratulate Dr. Strauss on the return of hair in the cured patches of lupus erythematosus on the scalp. In a late case which I had in a white woman of three or four years' duration, the hair completely regrew on two or three of the patches where previously they were absolutely hairless. I do not think that gold is a hair grower, but in curing lupus erythematosus it apparently has something to do with the hair follicles. It certainly has been an interesting observation in my case. Dr. Ketron's report is interesting. Through Dr. Schamberg I became interested over a year ago in gold and sodium thiosulphate. I have never had any reactions worth mentioning. I use the gold in rather large doses, usually starting with 50 and rapidly running up to 100 mg., using 100 once or twice a week, with an average of thirty or forty injections a year. I have had few reactions. In one case only a cutaneous reaction occurred.

DR. SIMPSON: I have followed several subacute cases. One case which I saw in Washington was not an acute one. There was some scarring of the fingers and lips. The lesion was not of the discoid type. The woman had been running a temperature. She had an arthritis. She had lesions on her face, neck, and some on her hands. At the time I saw her she did not

have fever but had considerable joint trouble, and was put to bed for that reason. I started the treatment with a mild dose of gold. I called up Dr. Wright, and on his advice started the patient on 10 mg. of the drug. The next day her temperature was 101 F. and rapidly increased to 103 F. The lupus erythematosus had greatly increased. The woman became toxic, developed a condition of the chest and died within a week. I report this case because it does not compare with anything else I have seen. I have cured practically all my patients with this gold preparation. It may have been an error in not allowing the condition to become more discoid and chronic before beginning treatment. I think this should be a clearing house where all difficult cases should be reported.

DR. WISE: I should like to hear Dr. Schamberg's opinion about acute, rapidly spreading lupus erythematosus of the trunk and extremities; what results he has had in its treatment, and whether he thinks it is dangerous to use the gold preparation in the acute stage.

DR. SCHAMBERG: I believe that one should proceed with extreme caution in cases of acute lupus erythematosus, or those associated with fever, because one may precipitate a fatal outcome. Recently I had a patient with lupus erythematosus who had been running a temperature of 101 and 102 F. for some months. She was thoroughly studied. Tuberculosis could not be found by radiographic and careful clinical studies. Her blood cultures were negative for septic organisms. Ten milligrams of gold sodium thiosulphate were given intravenously, and her temperature rose to 103 F. Fortunately a small dose had been used. Perhaps 100 mg. might have proved fatal. Her temperature gradually subsided. I advised treatment of ultraviolet light to the body, cod liver oil and hypernutrition. Later, by gradually increasing the dosage of gold, she was able to tolerate full dosage. Her fever disappeared and the lupus erythematosus likewise. Dr. Wright and I reported a fatal reaction in acute febrile lupus erythematosus. One must proceed with extreme precaution. Five or 10 mg. should be given and the result watched. An infinitesimal dose at the beginning is good practice.

Some one has asked what should be regarded as "acute lupus erythematosus." We usually mean a disseminate type, of short duration and rapid spread. Chronic cases may, however, present acute exacerbations. Our fatal case was one in which lupus erythematosus was present for several years with remissions and relapses; yet it was an acute disseminate type.

DR. STOKES: I would suggest adding to the criteria for regarding a case as threatening dissemination, the low leukocyte count. The extreme leukopenia is characteristic. The count goes down as the patient's condition becomes worse. I have seen counts as low as 1,300 leukocytes with a high fever. Patients whose leukocyte counts are below 4,000 are to be regarded as potential candidates for dissemination if given a therapeutic shock.

DR. SCHAMBERG: I wish to confirm Dr. Stokes' observation. The patient to whom I referred had a leukopenia.

SCROFULODERMA (?). Presented by DR. KNOWLES.

F. S., aged 19, white, an American nurse, presented a dermatosis on the right ankle, unassociated with subjective symptoms. The condition is of three or four years' duration. It was a pinkish mark for a while. Since last summer it began to discharge.

The patient has had three roentgen-ray treatments; emplastum plumbi and petrolatum. The result was the scarlike area larger than a silver dollar with a brownish edge. The biopsy scar was present.

DISCUSSION

DR. HIGHMAN: I think this is too important a case to be allowed to go without comment. Evidently there was some doubt as to the diagnosis. The

condition presented today was a yellowish, somewhat swollen, festooned plaque on the ankle, surrounded by a narrow zone that looked rather brown. The upper fold of this seemed like an irregular oyster-shaped lesion. It is here described as an ulcer. I do not see the point in this. I think perhaps the ulcer as shown was a result of the biopsy. There are two elements in the lesion that require consideration: the central, elevated, yellowish scar and the margin. The two together form a picture of the sort of disturbance which is seen in cases of morphea. The microscopic section unfortunately was not clear. What you could see looked like epithelial pearls. If this is malignant, then it is epithelioma, clinically presenting the appearance of morphea. Nine years ago Prentiss wrote an article on this condition. I do not think a body of this sort ought to accept a diagnosis of scrofuloderma.

DR. WEIDMAN: I wish to remark about just one phase of the picture: the yellow center. There is a condition known as "elastic degeneration in scars" in which this yellowing is known to take place. Dr. Ketron showed a case in Baltimore last spring. This yellow degeneration may occur in a wide variety of different scarlike structures.

A CASE FOR DIAGNOSIS. Presented by DR. CORSON.

O. S., aged 43, white, an American farm laborer, presented a generalized dermatosis especially involving the head, accompanied by moderate itching. In January, 1926, a peasized papule appeared in the center of his lower lip. In March, a heavy scab formed over his entire lower lip. Pus accumulated under the crust, and beneath the crust the lesion presented a granulomatous appearance. A similar condition developed at the back of the neck, where a sharply defined elevation area became slightly fungating and increased until it affected most of the scalp. Some large pustules appeared on other portions, as over the clavicles, elbows, wrists, ankles and feet. He had taken much potassium iodide before admission and had had many roentgen-ray treatments without effect. The drug was given after the eruption appeared. Histologic sections showed only a chronic inflammatory tissue.

The laboratory observations were: Absence of fungi; blood Wassermann, negative; traces of iodine and bromine in the urine; hemoglobin, 80 per cent; red blood cells, 4,230,000; white blood cells, 7,800; urine, negative. A culture from lesions showed *Staphylococcus albus,* and diphtheroid bacilli. A roentgenogram of the chest was negative.

DISCUSSION

DR. SCHAMBERG: I believe this case is dermatitis herpetiformis of the pustular type. It is not always possible to definitely differentiate this from a pemphigus. This man had had the eruption for two years. His general health was good. There were circumscribed patches of eruption on the chest, thighs, and other parts of the body. He has been made distinctly worse by the administration of iodine. This is one of the points of differentiation between the two diseases to which considerable importance is attached abroad. You will recall that many years ago Kaposi regarded dermatitis herpetiformis merely as pemphigus, but after many years physicians have accepted Duhring's disease.

DR. SIMPSON: The condition is an iodide eruption. The lesions on the legs and thighs were much more distinctive than the lesions on the chest and head. The patient gives a history of taking several bottles of medicine before the eruption appeared. It was made worse by the subsequent administration of iodide.

DR. WEIDMAN: Is the iodine still present in the urine? This patient was shown a long time ago before the Philadelphia Dermatological Society and some statement about iodism was made. Many months have elapsed and still the lesions continue to appear.

Dr. Corson: This patient has not been seen since he was discharged from the hospital some months ago, until he was presented today. He took rather large doses of potassium iodide one year before presentation, and when he was admitted to Jefferson Hospital he still showed traces of iodine in his urine. When we first saw the case it appealed to us as pemphigus vegetans, but the suggestion of iodism was strong. In all the time that has elapsed, however, the iodine should have been eliminated. Blastomycosis had been thought of, but search for blastomyces and histologic studies ruled this out.

Acanthosis Nigricans. Presented by Drs. Knowles and Ludy.

V. C., aged 14, an Italian, presented a universal dermatosis most marked in the axillary region, the groins, neck and trunk. In these regions the skin was verrucous and presented a corrugated appearance. There was a generalized pigmentation most marked in the verrucous areas.

The laboratory examination revealed: Occult blood in the stools; blood sugar, .1, and blood urea, 14 mg. The blood count was as follows: Hemoglobin, 90 per cent; red blood cells, 4,340,000; white blood cells, 11,400; polymorphonuclears, 59 per cent; small lymphocytes, 28 per cent; large lymphocytes, 8, and transitionals, 3. The basal metabolism was 15 per cent subnormal. The Wassermann test of the blood was negative.

The condition has improved under the administration of thyroid extract.

DISCUSSION

Dr. Weidman: Dr. Ludy asked me to state that a laparotomy had been performed on this patient. Neoplasm was not found, but there was tuberculous disease. I do not know the exact organ affected.

A Case for Diagnosis. Presented by Drs. Schamberg and Wright.

G., aged 26, presented a generalized eruption of one and a half years' duration. The patches were discrete erythematous, edematous, not sharply marginated and noninfiltrated. There was severe pruritus.

The condition did not improve under treatment with roentgen ray, quartz lamp therapy, or local remedies.

DISCUSSION

Dr. Wise: This case occasioned much discussion of an informal nature. It is one of the most difficult cases in all the wonderful display today. The diagnosis of seborrhoeic eczema was bandied about. This case had a history of a year and a halfs' duration with recalcitrance to roentgen-ray treatment, whereas seborrhoeic eczema would have responded. There was an absence of scaling in the scalp. He said that he has moderate itching. At a distance, the condition resembled seborrhoeic eczema or seborrhoeic dermatitis. When looked at closely, however, especially the lesions on the thighs, the presence of edema seems to be marked. Some of the lesions were actually elevated. These elevated lesions looked much like an "Adalin" eruption or an eruption due to cold tar products; yet the history was negative with regard to these products. The man denied having taken medicines of any kind except milk of magnesia occasionally. I had to eliminate antipyrin eruptions. I should offer tentatively a diagnosis of mycosis fungoides.

Dr. Lord, Baltimore: I also made a diagnosis of mycosis fungoides.

Dr. Wright: This man had a roentgen-ray treatment on only one occasion. He was given a skin unit to two or three areas on the back. That was last April or May. He said that he did not get better. We did not see him again until yesterday. That is all we know about the case.

Addendum.—This patient has subsequently improved 75 per cent following the application of a half skin unit of roentgen-ray therapy over the areas involved and the conjoint use of a crude coal tar ointment.

Carroll S. Wright, M.D., Secretary.

NEW YORK ACADEMY OF MEDICINE, SECTION ON DERMATOLOGY AND SYPHILIS

Regular Meeting, Dec. 6, 1927

E. R. MALONEY, M.D., *Chairman*

PARAPSORIASIS (TWO CASES). Presented by DR. BLOOM.

G. G., aged 65, born in Ireland, who came to the New York University and Bellevue Clinic on November 30, gave a history of an eruption which he had first noticed two months previously. It consisted of closely aggregated, pinkish, oval and round patches of various sizes, which were not infiltrated and were covered with a fine scale. The eruption was limited to the thighs (flexor and extensor surfaces) and was only slightly pruritic. The general condition of the patient was good. His previous history was negative. A biopsy examination made by Dr. Highman confirmed the diagnosis.

F. J., a boy, aged 7, came to the same clinic on October 17, with an eruption of four months' duration, consisting of macules and papules, appearing on the neck, trunk, upper and lower extremities, anteriorly and posteriorly. The macules, which were red-brown and lentil to dime-sized, were covered with a fine scale, which could be scratched off without producing bleeding points. The papules, ranging in size from that of a lentil to that of a small pea, were slightly infiltrated and a brownish red. The skin presented a mottled appearance with pigmented spots and lighter skin between.

According to the history given by the mother of the boy, the eruption had shown exacerbations and remissions, but had never disappeared entirely. The child had measles at the age of 2 and mumps at the age of 5. He was in good health when he applied to the clinic. The biopsy examination made by Dr. Highman confirmed the diagnosis of parapsoriasis.

DISCUSSION

DR. HIGHMAN: The second case, clinically, is suggestive of urticaria pigmentosa almost as much as parapsoriasis. The older lesions suggest the flat form of parapsoriasis, and this is verified by the microscope.

DR. FRASER: I agree with the diagnosis in both cases. Some of the lesions on the boy resemble those of urticaria pigmentosa. Nevertheless, I should make a diagnosis of parapsoriasis, disregarding the histologic picture. The walnut-brown color so characteristic of urticaria pigmentosa is absent from the majority of these lesions, and the scaling which is present here is not a feature of urticaria pigmentosa.

LEPROSY. Presented by DR. SAUNDERS.

M. E., a negro woman, aged 21, from the New York University and Bellevue Clinic, said that about ten years before presentation pain had suddenly developed in the right ankle, gradually spreading to the toes and to the other foot. The condition would disappear in summer and return during the cold weather until a few years before presentation, when it had become constant. Five years after onset, similar pain had developed in one of her fingers, which had followed a similar course as the pain in her feet, and had spread to the other hand. Gradually her fingers and toes had become constricted at the phalangeal joints, the terminal phalanges swelling and becoming painful and tender. One year later, she had developed a "sore" in the left nasal cavity, which had discharged profusely and obstructed her breathing. This had persisted for several years. During the year prior to presentation, reddish-brown areas about 0.5 cm. in diameter with underlying infiltrations appeared on her arms and legs.

On admission to the clinic she had on her arms a dozen intradermic infiltrations, each about the size of a pea, hyperesthetic, with a circumscribed over-

lying erythema. The infiltration had disappeared under treatment, and the overlying skin had become depigmented. She also had three erythematous areas, 1 cm. in diameter, on her right cheek, which were of a year's duration and which had persisted in spite of treatment. Results of the bacteriologic examination were negative. The histologic picture was that of leprosy.

There was no palpable nerve enlargement. Under treatment with the ethyl esther of chaulmoogra oil she had showed steady improvement.

DISCUSSION

DR. HOPKINS: It seems to me that the diagnosis should be made by neurologic methods. The woman has dystrophy of the phalanges; I could not tell from the examination I was able to make whether she had characteristic anesthesia. I think the possibility of syringomyelia or other diseases of the spinal cord must be ruled out before accepting the diagnosis of leprosy. I do not think the absence of bacilli in the lesions is important. The lesions, if leprous, are of the maculo-anesthetic type in which bacilli are rarely found.

DR. HIGHMAN: Microscopically, the lesions are those of ordinary leprosy. They are flat, granulomatous lesions macroscopically, while microscopically, as stated, they have all the characteristics observed in leprosy, with the exception of the bacillus. Unfortunately, the bacillus was not found, but I ascertained that the tissue was fixed in formaldehyde instead of alcohol; although that does not entirely exclude the possibility of finding bacilli, it increases the difficulty in finding them. Histologically, the lesions do not look like the lesions of the maculo-anesthetic type. I believe the patient has a combination of the cutaneous and nerve form of leprosy, and that syringomyelia will not prove to be the correct diagnosis.

URTICARIA PIGMENTOSA. Presented by DR. BOENKE.

J. De G., a boy, born Aug. 5, 1927, was presented before the University and Bellevue Clinic with the following history. Two weeks after birth the mother noticed three bullae on the inner aspect of the right thigh, each surrounded by a reddened area of the skin. These lesions healed within three weeks, leaving a normal skin. One month after the appearance of the lesions mentioned above, reddish wheals appeared on the thighs and legs, and the eruption then gradually extended to the rest of the body. The mother said that none of these later lesions had disappeared.

When first seen at the clinic on Nov. 17, 1927, the patient had a generalized eruption consisting of dark reddish, more or less oval, macular lesions, varying in size from that of a split pea to an inch (2.5 cm.) or more, many of the larger ones having a finely wrinkled appearance; associated with these were numerous wheals varying in size.

On November 30, there was practically no change in the older lesions beyond a slight change in color, but many new wheals were present. One on the left arm was surrounded by a bean-sized, tense, serous-filled bulla, while on the back of the neck and on the left leg were the remains of ruptured bullae. Itching, while present, had not been prominent.

DISCUSSION

DR. WALZER: To my mind, this is a case of urticaria pigmentosa, though the urticarial symptoms are unusually severe. The questions for discussion should be those that are still in dispute in this disease. 1. What is the relation of the mast cells to urticaria pigmentosa? 2. What is the relation of the pigmentation to the mast cells? 3. What is the relation of the urticaria to the disease? 4. When should the patient be considered cured: when no lesions develop, when the urticaria is gone, or when the pigmentation has disappeared? Of course there are some who claim that all or some of these questions have been settled, probably only to their own satisfaction, but not to the general dermatologic public.

DR. HOPKINS: I would like to ask Dr. Fraser whether there is any advantage in taking biopsies in the urticaria stage or when the lesions have been irritated?

DR. FRASER: I have examined sections from about a dozen patients with urticaria pigmentosa, both infantile and adult types, and was able to demonstrate mast cells in excess of the normal in all of them.

I should hesitate to call any case urticaria pigmentosa in which mast cells could not be demonstrated after repeated examinations. In reply to Dr. Walzer's questions: 1. The pigment is not present in the mast cells, it is in the perivascular connective tissue cells. 2. The mast cells in the urticaria pigmentosa arise locally from connective tissue cells and are not related to the mast cells of the blood. In reply to Dr. Hopkins' question, my experience has been that irritation does not increase the number of mast cells present, either in the lesions or in the surrounding skin.

DR. HIGHMAN: If any are really interested, I would commend to them a study on urticaria pigmentosa by Hartzell, published I think in 1915. It points out when, where and how the mast cells are found, the relationship between evolving and resolving lesions, the relationship to pigment and other points inquired about. They were amply discussed by Hartzell ten or twelve years ago, and nothing better has been written since. Incidentally, I do not think this patient has urticaria pigmentosa. I have never seen bullous lesions in this disease.

DR. POLLITZER: I have never seen urticaria pigmentosa with such enormous lesions. There are lesions more than an inch in diameter. It would be well to have a biopsy made.

PIGMENTATION OF THE BUCCAL MUCOUS MEMBRANE. Presented by DR. COOMBES.

G. P., a man, aged 50, a native of Asia Minor, from the University and Bellevue Clinic, presented a diffuse, patchy, bluish-black, confluent pigmentation of the mucous membrane of the cheeks, gums, and buccal surface of the lips of the canine type. On the soft palate were several isolated solitary pigmented spots, which showed up in marked contrast to the surrounding normal mucous membrane. The condition had been of about twenty years' duration. The patient had an arrested case of pulmonary tuberculosis. There was no history of bismuth, arsenical or mercurial therapy. He also had several annual lesions of erythema multiforme on his left shoulder of a week's duration.

A CASE FOR DIAGNOSIS (TUBERCULID?). Presented by DR. BECHET.

J. K., man, aged 19, from the University and Bellevue Clinic, had noticed a swelling on the right side of the neck three weeks previously. He had had an intermittent temperature, with malaise and pain in the various joints since that time. He presented numerous enlarged glands on both sides of the neck, with a soft boggy swelling, running along the right sternocleidomastoid muscle. On the rest of the body were a few infiltrated, pea-sized papules, some with a circinate border, others having broken down leaving brownish pigmented patches with slight necrotic center. On the penis were a few similar lesions covered with crusting.

DISCUSSION

DR. PAROUNAGIAN: I examined the patient carefully, and the best suggestion I can make is that he has a chancre situated somewhere in his throat, perhaps below the tonsil on the swollen side. The duration of the condition is too short for tuberculous glands. He has scattered lesions on the body and marked adenopathy. I would be interested in his Wassermann test.

DR. WOLF: The glands on the right side of the neck are soft and have the appearance of tuberculous adenitis. The lesions on the body appear to be tuberculids, in other words, the lesion is a papulonecrotic tuberculid. He also

has enlarged glands in the axillae. In view of the fact that the glands are soft, I ruled out Hodgkin's disease. The lesions seem to be necrotic, and do not suggest syphilis.

DR. COOMBES: I am inclined to agree with Dr. Wolf that the lesion is a tuberculid; the glands in the neck appear to be too soft for an adenitis due to chancre. The man has an abscessed tooth which may have caused the adenitis. The dentist is going to remove the tooth.

A CASE FOR DIAGNOSIS (TUBERCULOSIS?). Presented by DR. TULIPAN.

C. W., aged 40, born in the United States, from the University and Bellevue Clinic, in 1922 following a nasal operation noticed that his upper lip became markedly swollen, which condition lasted for almost three years. The swelling finally subsided after some local applications and light therapy. Beginning in August, 1927, the lower lip became swollen to almost four times its natural size, and ulcerations developed below the lip, extending almost from the corner of the mouth to the median line. Numerous Wassermann tests of the blood and spinal fluid taken at the Veterans' Hospital gave negative results.

The lower lip showed marked induration and swelling, with a dime-sized, hard, indurated and thickened lesion on the left side. At the right angle of the mouth was an ulceration with an irregular, punched-out, white border, and unhealthy granulations at the base.

On the inner side of the lower lip and base of the tongue were small ulcers and milky white patches.

DISCUSSION

DR. CANNON: I think that the enlarged, indurated, nonpainful glands of the neck, the verrucous infiltration of the mucous membrane over the hard palate and the firm elephantiasis-like swelling of the lips are characteristic of tuberculosis rather than of syphilis. I suggest that the patient's lungs be examined for evidence of tuberculosis.

DR. ROSEN: My first impression was that the condition was lupus vulgaris, for I thought there were distinct nodules on the under surface of the lip. This type of tuberculosis, however, does not involve such a large area in such a short time. Occasionally one sees tertiary syphilitic lesions in this location with secondary lymph stasis. This would account for the marked tumefaction of the involved area.

DR. MCCAFFERTY: I would like to suggest the diagnosis of lupus erythematosus of the lower lip. The lesion on the roof of the mouth does not of course correspond to the clinical picture of lupus erythematosus. It is possible that we may be dealing here with a true tuberculosis on the roof of the mouth and lupus erythematosus on the lower lip. I should like to see one of the preparations of gold tried on this patient.

IDIOPATHIC ATROPHY. Presented by DR. HALPIN.

F. L., a woman, aged 25, from the University and Bellevue Clinic, had a palm-sized patch on the right calf, which started three and a half years prior to presentation. This was a light pink, and throughout the entire patch were atrophic striae. At the border were several pinhead-sized white atrophic spots. On the left leg were a few irregularly shaped erythematous patches, which were slightly infiltrated but not painful.

TUMEFACTION OF CHEEKS. Presented by DR. COOMBES.

F. N., a Japanese, aged 42, from the University and Bellevue Clinic, had previously been presented at the November meeting of the New York Dermatological Society when his condition had been diagnosed solid edema. The condition had improved considerably under high voltage, heavily-filtered roentgen-ray treatments, but suggestions for further therapy would be appreciated.

DISCUSSION

DR. CANNON: I suggest surgical treatment.

A CASE FOR DIAGNOSIS (MELANOMA?). Presented by DR. THORNLEY.

E. M. W., aged 58, born in the United States, married, a laborer in the post office department and who was from the service of Dr. Fox at the United States Marine Hospital, No. 70, said that his present condition began a year and a half prior to presentation when he bruised and excoriated the distal phalanx of the left thumb. This was followed by the usual black nail, which he opened three months later, and in which he found only dried black blood. The thumb remained uncomfortable, and two months later the whole nail was removed. The thumb remained tender, and several months later the present growth appeared.

Examination showed a raw, fungating mass, the size of a small walnut, occupying the site of the left nail. The color was black with red and gray mottling. The edges overhung in places and showed a tendency to pedunculation. The edges of the surrounding skin were not indurated, but were sharply defined from the tumor mass.

Roentgen-ray examination of the thumb showed moderate rarefaction of the distal phalanx and slight rarefaction of the proximal phalanx, due to low grade osteomyelitis of the distal phalanx. Several Wassermann tests were negative. The diagnosis appeared to be either melanoma or pyogenic granuloma.

DISCUSSION

DR. ROSEN: I have seen two or three patients with a similar condition, which is usually malignant. Those that I observed had melanocarcinomas which terminated fatally within the year. This type of lesion metastasizes rapidly, and surgical intervention, no matter how early or how radical, is of no avail.

DR. OULMANN: About twelve years ago, I showed a patient with melanocarcinoma of the thumb at the Manhattan Dermatological Society. The present patient shows almost an identical lesion. My patient succumbed to intestinal and stomach metastases about three years after the onset of the original tumor.

DR. POLLITZER: Attention was first called to these cases by Jonathan Hutchinson. This case is quite typical. The man met with an accident to his thumb; it was not badly injured, and was entirely healed within the course of a week or two. A few months later, he noticed a black streak creeping up under the nail, and presently a little swelling occurred under the free edge of the nail, which developed into the walnut-sized tumor now present. Probably the man had a congenital deposit of a melanotic character under the nail, and the injury caused it to become active. The cases are necessarily fatal. I imagine that if his thumb or his arm had been amputated early after the appearance of the black streak he might have been saved, but at this stage it is almost certain to be fatal with a general melanosis.

A CASE FOR DIAGNOSIS (DERMATOPHYTOSIS?). Presented by DR. SCHEER.

G. L., aged 72, housewife, born in Russia, from the Post-Graduate Clinic, presented a lesion on the left forearm, which she had had for a year and a half. The lesion was circinate, occupying the anterior surface of the lower half of the left forearm, and extending backward over part of the dorsum of the wrist. It was sharply defined, pinkish-red, with a raised scaly border; the average width was one eighth of an inch (0.3 cm.). The center part was composed of partly clear and partly scaly papules. The lesion itched severely. There was, also, pruritus with lichenification on the flexors of the elbows.

DISCUSSION

DR. HALPERIN: Clinically it seems to be a fungus infection of the skin.

SPINDLE CELL SARCOMA CUTIS. Presented by DR. OULMANN.

L. P., aged 52, about fourteen years before presentation noticed a small hard nodule on his chest. Others appeared slowly within the next ten years. They attained the size of a pea. Two lesions were excised and studied microscopically by Unna, who made a diagnosis of spindle cell sarcoma.

Over the sternum on a level with the fourth and fifth ribs on both sides, for a space of 5 by 2½ inches, the skin was infiltrated, and contained a number of hard, pea-sized nodules fixed in the skin. The skin was freely movable from the sternum. The fourth ribs on both sides were thickened.

BOECK'S SARCOID. Presented by DR. HOPKINS.

P. Y., aged 43, who was born in Germany and had lived fifteen years in this country, had never been seriously ill and had not had any disease of the lungs or glands; nor was there any history of tuberculosis in the family.

The eruption began nine years before presentation on the forehead, with yellowish small papules which later turned red. Patches were formed by coalescence of these papules, which cleared up in the center to form rings. The lesions never ulcerated. New lesions appeared constantly. The Wassermann test was repeatedly negative. A biopsy showed tubercle formation in the cutis.

DISCUSSION

DR. HIGHMAN: I do not think it is definitely settled that this is Boeck's sarcoid. If we refer to a posthumous article by Boeck in the *Archiv für Dermatologie und Syphilologie* in 1918, we discover that the author who first used the term sarcoid regrets the word and suggests the designation of miliary lupoid. I do not think the substitute is much better, but Boeck suggested it. In any event, the term miliary lupoid is applied to a definite picture, a discoid, dark red lesion, with gray lupoid milia. The lesions in the patient shown are identical with those in a case which has been shown periodically in Philadelphia. They are festoons progressing from a central point. Histologically, the structure shown is characteristic of tuberculosis. I think it is cavilling to split hairs as to whether a lesion of the skin which looks like granuloma annulare or lupus vulgaris in fine progressing lines, or miliary lupoid or any other type of tuberculosis should have this or that shallow, restricted interpretation. I do not think we are far from wrong if we call such a case lupus or miliary lupoid or any other name that might be applicable. It is certainly a case of progressing tuberculosis of the skin, and when one can analyze the essential lesions it looks as though they presented lupus nodules. Boeck points out in his article that in the typical cases of his particular type of lupoid, the nodules instead of looking like those in lupus vulgaris had a grayish color. I fancy that this is a rare form of cutaneous tuberculosis, and until it can be definitely fitted into a more definite group we should so consider it. I do not think it is Boeck's lupoid in the classic sense.

DR. HOPKINS: The case shows a remarkable resemblance to the case of Boeck's sarcoid pictured by Lewandowsky. The sections from the issue also show the discrete tubercles with giant cells which Boeck considered characteristic of this condition. Clinically and histologically, it is much closer to the cases described by Boeck and Lewandowsky than are those usually diagnosed as sarcoid. It seems useful to separate these conditions sharply from lupus vulgaris, for which the present case could hardly be mistaken. In the light of the present evidence, it seems probable that all of them are forms of tuberculosis of the skin. However, the tuberculous nature of sarcoid has never been proved; particularly in the absence of evidence of tissue destruction, it bears no resemblance to lupus. The prognosis is utterly different. For these and many other reasons, a sharp distinction is important.

LEUKEMIA CUTIS. Presented by DR. ANDREWS.

R. H., a chauffeur, aged 64, born in the United States, was first seen in the clinic on Nov. 9, 1927, complaining of itching of the face. He had suffered from this condition for the past year and a half. During his stay in the Memorial Hospital the condition disappeared, only to reappear when he returned to his home six weeks before presentation.

On the forehead were several quarter-sized, infiltrated, pinkish plaques. The cheeks showed a diffuse infiltration, partly nodular. There was a single nodule of hard consistency on the upper lip. The back and forearms showed numerous small, papular lesions, many of which had excoriated tops. The right inguinal lymph nodes were enlarged. The blood count revealed: hemoglobin, 55 per cent; red blood cells, 3,856,000; white blood cells, 3,500; polymorphonuclears, 57 per cent, and lymphocytes, 43 per cent.

DISCUSSION

DR. POLLITZER: The lesions are characteristic of leukemia cutis. What impresses me is the remarkable blood picture. The man is anemic and has a marked leukopenia; his white cell count is 3,500, but, if one contrasts the white cell count with the small red blood cell count (3,856,000), he has a relative leukemia of the blood.

BISMUTH STOMATITIS. Presented by DR. ROSTENBERG.

The patient was treated for secondary syphilis with eight injections of arsphenamine and eleven of bismuth salicylate. After the last injection, a distinct black line appeared on the gums, and bluish-black macules were noticed on the under surface and along the veins of the tongue. Some of the black lesions on the tongue ulcerated. There was a severe foetor ex ore. The patient was unable to eat solid food.

The patient was receiving sodium thiosulphate by mouth, and had seemingly improved under this treatment.

A CASE FOR DIAGNOSIS (MELANOMA?). Presented by DR. CANNON.

M. M., a colored bus boy, aged 57, born in Porto Rico, was first seen in the clinic on Dec. 6, 1927, with a lesion involving the tip of the nose. The history was not easily obtainable, owing to the patient's inability to speak English. The lesion apparently began nine months before presentation as a small spot on the tip of the nose, gradually increasing in size to its present dimension. Examination showed a lesion the size of a quarter which was bluish and deeply pigmented; the margins were not infiltrated, and seemed to blend with the adjacent tissue. The central portion was slightly elevated, with some scarring. There were two small pigmented moles on the left cheek and ear.

DISCUSSION

DR. FRASER: I understand from the history that the condition developed from a wart. If that is so, I feel that the present lesion is a malignant melanoma. There are no palpable lymph nodes, but that would not militate against the diagnosis of malignancy, as these tumors metastasize by way of the blood stream. The lesion should be removed radically, and sections examined microscopically.

DR. CHARGIN: I suggest lupus erythematosus as a possible diagnosis. The patch of eruption shows hyperkeratotic follicles, atrophy, scaling and pigmentation which, together with the duration, fairly well fits into the diagnosis suggested.

DR. ROSEN: I will make another suggestion; we have already had two. I do not know how to account for the bluish discoloration, unless it was produced by some topical application or was associated with a neoplasm. On

account of the irregular outline of the infiltration and the tendency to healing in some areas, I would suggest that the patient receive antisyphilitic treatment for two or three weeks before any radical procedure is carried out.

DR. WOLF: The lesion has a flat, noninfiltrated base with a tendency to atrophy in the center. There is no tumor that I know of that could be called a melanoma that is not raised from the skin. The pigmentation might be explained on the ground of a topical application in a colored person. The lesion does not look malignant to me.

DR. SHARLIT: I questioned the patient through an interpreter this afternoon. His history is that the pigmented lesion appeared first; that at no time did a protruding lesion such as a wart show itself; that the destructive lesion now present within the confines of the area of pigmentation developed on a smooth, flat skin. The patient further asserts that the lesion has not been treated in any way.

DR. BECHET: I agree with Dr. Fraser. The man has an outlying melanotic-like lesion on the cheek, near the one on the nose and another on the ear; both are as deeply pigmented as the nasal lesion. It might, then, be proper to assume that they are related. The pigmentation is blue-black, and the lesion on the nose is elevated. It seems therefore plausible to consider the diagnosis of melanosarcoma.

DR. MCCAFFERTY: I agree with the diagnosis of lupus erythematosus as suggested by Dr. Chargin. When lupus erythematosus is present in light-complexioned colored people, the periphery frequently is hyperpigmented. I believe that this hyperpigmentation only strengthens the diagnosis of lupus erythematosus in colored people.

DR. WISE: The case is of interest especially in regard to approach of treatment. Something has to be done for the patient. To me the diagnosis of melanoma does not seem a good one, that is, melanocarcinoma or sarcoma. The location is most unusual for that. The man is a Porto Rican, not a negro. I believe that any lesion in him might assume a dark color such as he presents. It seems to me that if he is to be treated, it would not do any harm to obtain a small piece of tissue for biopsy, examine it, and then go ahead with the indicated therapy.

DR. ROSTENBERG: My diagnosis is syphilis on a melanotic base.

DR. CANNON: It is evident from the discussion that a positive clinical diagnosis is impossible, and the only way we can definitely determine the cause of the lesion is by a biopsy study or a Wassermann test. We considered the possibility of such diagnoses as lupus vulgaris, lupus erythematosus, syphilis and melanocarcinoma. We thought that the duration of nine months' and the fact that the condition was limited to the tip of the nose without infiltration and without involvement of the mucous membrane of the nares were not suggestive of syphilis. Nodules were not present to suggest lupus vulgaris, although the contraction of the tissues producing a pigmented nose that is often seen in this condition was suggestive of lupus vulgaris rather than of lupus erythematosus. I have never seen a melanocarcinoma without tumor formation; furthermore, it is unlikely that such a condition could be present for nine months without evidence of metastasis. In this case, we have only the bluish color to suggest a melanoma. The two pigmented moles on his cheek I believed were in no way related to the lesion on the nose. I shall make a study of a biopsy and have a Wassermann test of the blood made; the results of both I shall report at a later meeting.

PARAPSORIASIS AND TUBERCULID. Presented by DR. ANDREWS.

Miss T. K., a radio assembler, aged 19, born in Austria, appeared first in the clinic on Nov. 28, 1927, complaining of a generalized eruption of the skin. About four years previously, a diffuse superficial rash first appeared on the inner aspects of both arms, and spread to the trunk and lower extremities.

This condition had persisted practically up to the time of presentation. About one year previously, the patient first noticed a dime-sized, pustular lesion on the right forearm, and since that time numerous similar lesions had appeared scattered over the trunk and extremities. She had used "black salve" on these lesions for two months. Other medication had not been used. The patient's appetite was good; bowel movements were regular; the weight was normal; menstruation was normal. She had had scarlet fever.

Scattered over the trunk, and especially on the flexor surfaces of the extremities, were pinkish, erythematous lesions, varying in size from that of a pinhead to that of a quarter, and covered with a fine superficial scale, which produced an atrophic appearance (pseudoatrophy) on the trunk. The lesions did not itch, and were less visible in summer time, but had never disappeared entirely.

On the extensor surfaces of the extremities, but also irregularly scattered over the trunk, were lesions of furuncular appearance, varying in size from that of a pea to that of a quarter. Fully developed lesions showed definite central necrosis and deep-seated subcutaneous infiltration. Around the elbows, and irregularly distributed on other parts of the body were "knitted" scars, varying in size from that of a lentil to nearly that of a quarter. There was marked acrocyanosis of the lower extremities. The case was presented as one of parapsoriasis guttate and papulonecrotic tuberculid.

DISCUSSION

DR. FOX: I agree with the diagnosis of parapsoriasis guttata.

DR. HIGHMAN: I would suggest that the so-called papulonecrotic lesions are ecthyma, infections caused by scratching.

DR. ANDREWS: The lesions on the extensor surfaces of the elbows and knees of five years' duration with scars are in the typical locations for papulonecrotic tuberculid. It does not fit in with my idea of ecthyma. I think that the case is a typical one of papulonecrotic tuberculid.

A CASE FOR DIAGNOSIS (GRANULOMA ANNULARE?). Presented by DR. CANNON.

B. W., a boy, aged 5, born in the United States, was first seen in the clinic on Nov. 11, 1927. One Wassermann test was 4 plus; several others were negative. Wassermann tests on the father and mother were negative.

Surrounding the left malleolus was an annular group of subcutaneous hard nodules, forming an irregular looped pattern. There was no change in the overlying epidermis. In places, infiltration was linear and indistinct, and in others nodular and shotty. There were two, hazelnut-sized, deep subcutaneous nodules, which seemed to be attached to the anterior border of the tibia. The patient had been taking iodides and mercury for a few days. It was necessary to differentiate between granuloma annulare and syphilis.

PHENOLPHTHALEIN ERUPTION (?). Presented by DR. CANNON.

Miss D. A., a colored woman, aged 21, born in the United States, a clothes presser, was first seen in the clinic on Nov. 25, 1927, with a lesion on the outer aspect of the right elbow which had been present about one year. The patient said that at one time the lesion became red and very itchy. She gave a history of using phenolphthalein laxatives for many years.

On the skin over the outer aspect of the right elbow was an oval lesion 3 by 1 cm. in diameter, dark brown and surrounded by a fine pinkish border. The Wassermann test of the blood was 4 plus. The Kahn test was 6 units.

DISCUSSION

DR. ABRAMOWITZ: The eruption that this patient presents conforms to the type produced by phenolphthalein, although it is rather unusual for the erup-

tion not to have spread after several relapses. For the sake of information, I would like to know whether any of the members have seen phenolphthalein rash in colored people. The only authentic case in the literature was presented by Dr. Oulmann at the Manhattan Dermatological Society recently.

DR. CANNON: This is the fifth time we have encountered this particular eruption in the colored race. In two instances, the lesions were not only on the body, but also on the glans penis.

RECURRENT ROSEOLA. Presented by DR. PAROUNAGIAN.

Mr. B., aged 26, was admitted to the Bellevue Clinic on Nov. 22, 1926, at which time he presented the following history: remains of anal chancre, roseola, condylomas about the anal region and a 4 plus Wassermann reaction.

He received fifteen injections of arsphenamine and fifteen of mercuric salicylate from Nov. 30, 1926, to March 1, 1927. His Wassermann test on April 18, 1927, was negative, though in June it became 4 plus. He did not return for treatment.

On Nov. 17, 1927, he returned with a general macular eruption arranged in annular form, the duration of which was said to be about six weeks. The Wassermann reaction of the blood was still 4 plus. New initial lesions were not presented.

DISCUSSION

DR. FOX: The chief interest in this case of roseola is not that it is recurrent, but that it assumes a circinate form, which is decidedly rare. This circinate macular syphilid is not to be confused with the comparatively common circinate papular eruption so characteristic of the negro race. The circinate macular eruption has been seen chiefly in women, and has been reported chiefly in Denmark and England.

DR. PAROUNAGIAN: When the patient was seen on Nov. 17, 1927, he presented a characteristic, generalized macular eruption which was annular, as is usual in this type of recurrent roseolas. He consented to be shown before this section, but during his absence, without my knowledge, he had been applying quartz light, as this treatment had been recommended to his sister who had tuberculosis. This to my surprise had cleared up the eruption on the body entirely, leaving some of the lesions on the arms where evidently the light had not been applied.

As to Dr. Fox's statement that these cases are rare, I must say that on the same afternoon another patient with even a better eruption than this one was seen. Unfortunately, when he returned this afternoon he had little to show. I recall showing similar cases before this Section and also at the Manhattan Dermatological Society.

Most of these cases occur within a year after infection, and the only exception was a patient, shown before this Section several years ago, who presented a recurrent roseola four years and seven months after infection.

DR. ANDREWS: The use of quartz light in the treatment of syphilis is being discussed in foreign literature and in this country. Not only is it useful for the stimulation of old tertiary lesions, but it is also employed in combination with arsphenamine in handling secondary cases. The generalized light baths for tonic effect are employed on neurologic patients as a routine by some well known neurologists in this city.

DR. ROSEN: I do not know anything about the ultraviolet rays in the treatment of patients with syphilis, but I think it is a dangerous procedure to produce an erythema of the surface of the skin during treatment with the arsenicals. In this way the drug is brought to the surface, and there is a strong possibility of producing an arsenical dermatitis.

DR. ANDREWS: Ultraviolet rays and roentgen rays are used successfully for the treatment of dermatitis produced by arsphenamine.

KAPOSI'S SARCOMA. Presented by DR. MCCAFFERTY.

A. L., a compositor, aged 61, born in England, was first seen in the clinic on Nov. 29, 1927, complaining of painful swellings on the toes of the left foot. He said that the first growth had appeared five weeks prior to coming to the clinic. This growth was removed by a chiropodist. One week later, several similar lesions appeared on the other toes of the same foot, and since that time the patient had developed about a dozen tumors in all. The lesions were moderately painful on pressure.

Between the toes of the left foot and on the end of the third toe the patient presented numerous lentil to small pea-sized tumors, which felt moderately hard and were covered with smooth, thin, violaceous colored skin. There were a few lesions on the sole and dorsum of the big toe; also diffuse edema of this region. The patient presented edema of the lower part of the left leg. The microscope showed hyperplasia of the fibrous tissue and dilated blood vessels.

DISCUSSION

DR. HIGHMAN: The histology as presented is not enough to base a diagnosis of Kaposi's sarcoma on. I shall be interested in seeing a detailed report of the case. Kaposi's sarcoma is microscopically angiofibrosarcoma with hemorrhages.

SARCOID. Presented by DR. HOPKINS.

Mrs. A. K., a stenographer, aged 28, born in the United States, referred by Dr. L. B. Robinson, first appeared in the clinic on Oct. 1, 1927, complaining of several small growths on the arms and legs. She said that the first lesion appeared on the right arm a year before coming to the clinic, and since that time about three dozen lesions had appeared on the legs and arms. The lesions were asymptomatic and never ulcerated. They appeared as slightly elevated, infiltrated, bluish-red papules, varying in size from 0.5 to 2 cm. in diameter. A biopsy showed tuberculoid granuloma.

J. J. ELLER, M.D., Secretary.

Book Reviews

HISTOCHEMIE DER HAUT. By PROF. P. G. UNNA, Hamburg. Paper. Price, 20 marks. Pp. 163, with 69 colored illustrations. Leipzig: Franz Deuticke, 1928.

In the study of the normal and pathologic events occurring in the skin, dermatologists no longer content themselves with the minute, faithful portrayal of the tissue changes presented by a histologic section. The description of the morphologic observations is supplemented with interpretations of the living processes accompanying and producing the alterations of the cellular architecture.

Unna was one of the first to engage in these investigations, and in the book under consideration he presents a survey of his contributions to the subject of the "Histochemistry of the Skin."

Applying to his own domain: the study of the skin, the basic principles of Ehrlich's "Farbenanalyse," that is, the analysis of the microchemical reactions of the tissues with the aid of stains, Unna endeavors to transform the histology of the skin into an experimental, intracellular chemistry of this organ.

In his task of eliciting the meaning of the biologic processes Unna does not confine himself to the employment of the technology of Ehrlich's stain, because this, according to Unna, results chiefly in a tinctorial characterization of the cell proteids, establishing their topical relations, without revealing their chemical properties.

Drawing on the methods of analytic chemistry, Unna systematically applies to the tissue sections a series of solvents, and associates with this procedure a technic of specific staining. This combination of methods called: "chromolysis" enables Unna not only to differentiate the acid from the basic groups of proteids, but also to define the group members according to their solubility.

The author emphasizes the indispensability of frozen sections for the elaboration of Ehrlich's hypothesis of the oxygen requirements of the organism, which resulted in Unna's discovery of the oxygen- and reduction-localizations in the structures of the skin.

In the book are also presented the author's and his collaborators' (Baudisch, Golodetz, Fezer, Wile, Ciliano, Lorberbaum, Schwenter, Unna, Jr.) studies of the integumentary fats, the plasma- and mast-cells, collagen, elastin and elacin.

Treating these various subjects from the standpoint of the "histochemist," Unna brings out new and stimulating aspects and records many observations which should prove valuable aids in developing a dynamic concept of normal and pathologic conditions of the body in general, of the skin in particular.

It is convenient to have the novel reagents and staining methods devised by Unna gathered in one book, and the collection of detailed directions for staining procedures will be welcomed by all who pursue histologic studies.

"Une science à faire" (a science in the making) calls for a new terminology and Unna, consequently, has coined a number of new denominations and endowed old terms with new meanings. The reader has to familiarize himself with these innovations before he can duly weigh and thoroughly appreciate the significance of the author's discoveries. Although he fully recognizes the privilege of the experimental investigator to link up the isolated facts of his discoveries with one another by generalizing hypotheses, the reviewer has to confess that he would have preferred it if some of the iconoclastic statements were less dogmatic and if the distinctions between the demonstrable and the speculative were more sharply drawn.

To the student who would like to round out his knowledge of the phase of dermatologic research represented by Unna's "Histochemie der Haut," the reviewer suggests the reading of "Lebensvorgaenge in der Haut der Menschen

und der Tiere" by Unna and Schumacher, Jesionek's "Biologie der gesunden und kranken Haut," and that illuminating treatise by Kyrle, "Histobiologie der Menschlichen Haut und ihrer Erkrankungen."

DISEASES OF THE SKIN. By HENRY H. HAZEN. Third edition. Price, $10. Pp. 572, with 248 illustrations. St. Louis: C. V. Mosby Company, 1927.

In this edition, Hazen has taken occasion to make a few additions necessary to bring his work entirely up to date. The most outstanding thing that one notices is that he has taken the bold step of omiting the subject of eczema as such. Many people have talked about this, but it has been left for Hazen to do it. It is not necessary to do more than call attention to the appearance of this third edition. The fact that there is a third edition indicates the satisfactory reception that the book has had. The author is to be congratulated one its completion.

LEHRBUCH DER HAUT-UND GESCHLECHTSKRANKHEITEN. By EDMUND LESSER. Pp. 467. Berlin: Julius Springer, 1927.

Attention is called to the appearance of this second volume, the volume on venereal diseases, of the fourteenth edition of Lesser's "Handbook," edited now by Professor Jadassohn. It is, of course, one of the long established works on the subject, and it is not necessary to say that, under the editorship of Professor Jadassohn, it maintains its high standard.

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